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ACCLIMATIZATION VERSUS TOLERANCE TO STRESS

An Annotated Bibliography

Volume I

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FOREWORD

This bibliography was compiled by members of the Life Sciences Department, Space and Information Systems Division, North American Aviation, Incorporated, Downey, Calif., under task No. 793002 and contract No. AF 41(609)-2335. The program was begun in May 1964 and completed in July 1965. The work was monitored by personnel in the Environmental Systems Branch, USAF School of Aerospace Medicine. The material was submitted for publication on 20 July 1967.

The bibliography is in two volumes. Section I, "Acclimatization and Chronic Hypoxia," is incorporated in this volume. The second volume contains bibliographic information related to "Acute Hypoxia," "Decompression," "Hypercapnia," and "Hyperthermia."

This report has been reviewed and is approved.

GEORGE E. SCHAFER
Colonel, USAF, MC
Commander

ABSTRACT

This bibliography was prepared from the literature surveyed as part of the study to determine the effect of altitude acclimatization on various selected stresses. This volume contains a compilation of titles and abstracts on altitude acclimatization and the exposure to chronic hypoxia. The bibliography is arranged alphabetically by last names of authors.

INTRODUCTION

The physiological desirability of the composition of a space cabin atmosphere is usually assumed to bear a direct relationship to the closeness with which the given atmosphere approximates the earth's sea-level atmosphere. Deviations from this thesis have included suggestions of hypothermia for the reduction of metabolic rate, the substitution of other inert gases for nitrogen to reduce the potential for the bends, and finally an atmosphere equivalent to one which produces altitude acclimatization in mountain dwellers. This last consideration is of interest here.

From the early work of Mosso, Bert, Muller, Barcroft, Haldane, to the more recent work of Hurtado, Chiodi, Merino, Kellog, Dill, etc., evidence has accumulated to show that the body, through various physiological adaptations, produced over a period of time, is capable of carrying out normal activities at altitudes from 12,000 to 18,000 feet. Previously acclimatized crewmen operating in a cabin atmosphere equivalent to 12,000 to 15,000 feet of altitude should, therefore, show no decrement in normal performance. Of primary interest is the comparison between the tolerance of the acclimatized crewman to various other stresses imposed by the mission, either accidental or anticipated, and the tolerance of the unacclimatized crewman operating in a normal oxygen environment.

Stresses such as acute hypoxia, hypercapnia, decompression, hyperthermia, acceleration, and exercise could be expected to occur most commonly during space flight.

Experimental evidence indicates that acclimatization to altitude significantly increases tolerance to acute hypoxia and to decompression. The other stresses have not been thoroughly investigated. The purpose of the present study is to establish a relationship between the physiological changes of altitude acclimatization and tolerance to the above-listed stresses.

Preliminary to the formulation of an experimental program, attempts have been made to establish theoretical relationships between physiological changes of altitude acclimatization, changes produced by acute exposure to each stress, and changes produced by a prolonged exposure to each stress. The literature which was utilized in the establishment of these relationships is presented here in the form of an annotated bibliography.

I. ACCLIMATIZATION AND CHRONIC HYPOXIA

A

Abramson, D. I., S. M. Fierst, and K. Dachs. Resting peripheral blood flow in the anemic state. Amer. Heart J. 25:609 (1943).

Adam, J. M., et al. Further experiments on naturally acclimatized men. Med. Res. Counc. Spec. Rep. (London) 298:29-38 (1960).

Adam, J. M., et al. The effects of environmental stress: Measurements on artificially acclimatized men. Med. Res. Counc. Spec. Rep. (London) 298:39-74 (1960).

Adler, H. F. Abdominal symptoms at altitude. AF School of Aviation Medicine, Project No. 493, Report No. 1, Randolph AFB, Texas (16 June 1947).

Adlersberg, D., and O. Porges. Blood oxygen in high altitude. Klin. Wschr. 2:2209-2210 (16 Nov. 1923).

Adolph, E. F. General and specific characteristics of physiological adaptations. Amer. J. Physiol. 184:18 (1956).

Agadzhanian, N. A. Apparatus for registration of blood pressure in high altitudes. Voennomed. Zh. (Moscow) 10:87-89 (Oct. 1958).

Agadzhanian, N. A. Extinction of conditional electro-defensive motor reflexes in a rarefied atmosphere. Zhurnal Vysschei Nerundi Deiatel'nosti, 6(2):260-268 (Mar.-Apr. 1956). Dogs conditioned to defensive motor reflexes at the sound of a bell were subjected to decompression to altitudes of 6000 and 8000 meters. The extinction of the reflexes was studied and interpreted in Pavlovian terms. Conclusion: the mechanisms of extinction involved the weakening of cerebrocortical cells in acute hypoxia.

Agostino, B.A. d'. Thyroid iodine and muscular fat in animals raised at various altitudes. Arch. Sci. Biol. 35:583-591 (Nov.-Dec. 1951).

Albaum, H.G., and H.J. Chinn. Brain metabolism during acclimatization to high altitude. Amer. J. Physiol. 1:141-145 (July 1953). Acclimatization of rats to lowered barometric pressure (equivalent to 11,000, 18,000, and 22,000 feet) did not significantly alter the levels of the determined brain constituents. The following portions were determined: inorganic P, phosphocreatine, organic P, glycogen, lactic acid, adenylic acid, adenosine diphosphate, adenosine triphosphate, hexose diphosphate, glucose-1-phosphate, and diphosphopyridine nucleotides. The hemoglobin rose markedly in rats maintained at 18,000 and 22,000 feet.

Albaum, H.G., and H.H. Chinn. Enzyme studies in acclimatization to high altitude: I. Brain metabolism during altitude acclimatization. AF School of Aviation Medicine, Project No. 21-1201-0009, Report No. 1, Randolph AFB, Texas (May 1953).

Albaum, H.G., W.K. Noell, and H.J. Chinn. Enzyme studies in acclimatization to high altitude: II. Chemical changes in rabbit brain during anoxia. AF School of Aviation Medicine, Project No. 21-1201-0009, Report No. 2. Randolph AFB, Texas, (June 1953).

Albers, D. and A. Koch. Changes in electrocardiogram at high altitudes. Zeitschrift Kreislaufforsch. 33:142-153 (1 March 1941).

Alexeef, A.J. Effect of mountain climate on catalase of blood. Biochem. Z. 192:41-57 (1928).

Aliev, M.A. On the therapeutic properties of the mountain climate in hypertonia. AFSC, N65-17833. Foreign Technology Div., Wright-Patterson AFB, Ohio (24 Nov. 1964). Renal form of hypertonia was produced in dogs by collapsing one or both kidneys with a rubber capsule. Under conditions of high altitude (1800 meters), hypertonia was recorded in the dogs in which unilateral renal ischemia had been produced. At altitudes of 2700 meters above sea level, a delaying effect was also observed. This retarding influence was verified at 3200 meters. Hypertonia did not develop in any of the dogs with one kidney collapsed. Collapsing both kidneys resulted in an increase in arterial pressure. Thus, the climate of high mountains, which constitutes a complex of atmospheric factors (subnormal barometric pressure, intense sunlight, negative air ionization, moderate temperature) had a therapeutic effect on induced hypertonia.

It was noted that favorable therapy was not experienced during the cooler weather in the mountains (September to October).

Alifanov, V.N. Changes of motor conditioned reflexes in man in conditions of hypoxic hypoxia and low barometric pressure. Zh. Vyss. Nerv. Dejat. Pavlov, 11:28-33 (1961). The effects of hypoxic hypoxia low barometric pressure on the motor conditioned responses (CR's) of man were studied. The effect of hypoxia was achieved by keeping the subjects in a rarefied chamber (5,000 meters) for 30 minutes, while they breathed the air about them. The effect of low barometric pressure was achieved by "elevating" the subjects in a pressure chamber to an "altitude" of 10,000 meters for 20 to 25 minutes, while they breathed O_2. The author finds that with good tolerance of moderate hypoxia there is no marked impairment of the active inhibitory processes. Stability of the latent CR's at the altitude suggests fairly strong processes of excitation and inhibition in the cerebral cortex. In these cases the signs of protective inhibitions are also absent, indicating fairly stable adaptation of the central nervous system's functions to hypoxia. The changes noted in conditioned activity resemble barometric pressure, especially with the deterioration of the condition of the subjects. Both of these unusual environment factors are able to provoke a general adaptation-compensation reaction of the body. There is also reason to believe that in both cases some degree of O_2 deficiency develops, although the origin is different. In the former case, the O_2 deficiency is caused by a low partial pressure of O_2 in the inspired air; in the latter case some form of circulatory hypoxia may set in as a result of functional impairment of the cardiovascular and respiratory systems.

Alifanov, V.N. The effect of hypoxia and low barometric pressure on the motor and sensory chronaxie in man. Biull. Eksp. Biol. Med. 41(1): 29-32 (1956). Translation.

Allegretti, A. J. Blood pressure as affected by altitude. Med. Bull. Veterans Admin. 19:290-291 (Jan. 1943). The influence exerted by differences in altitude upon normal blood pressure in similar persons in similar circumstances is studied by the author, who was transferred from the facility at Hines, Ill., where the altitude is 650 feet, to the facility at Cheyenne, Wyo., which is 6105 feet above sea level (a difference of 5500 feet or well over a mile).

Altland, P. D., and B. Highman. Effects of high altitude on cholesterol-fed rabbits. Production of severe pulmonary atherosclerosis with calcification. Arch. Path. 70:340-357 (Sept. 1960). The occurrence after exposure to high altitude of fatty changes in the arterial media of rats and non-lipid arteriosclerotic lesions in the aorta of dogs lends support to the theory that anoxemia may be a predisposing factor in the production of arteriosclerosis. Further study of the role of hypoxia in the production of arteriosclerosis is warranted. In this study, the effects of exposure to high altitude on the character and distribution of atherosclerotic lesions in cholesterol-fed rabbits has been studied.

Altukhov, G.V. Studies on higher nervous activity in men in the condition of a prolonged exposure to rarefied atmosphere, Zh. Vyss. Nerv. Dejat Pavlov, 11:582-592 (July-Aug. 1961).

Alzamora, R., and C. Monge. Electrocardiographic modifications in the Andean during his adaptation to sea level. An. Fac. Med. (Lima) 38(1):65-73 (1955). Electrocardiographic tracings of Andean natives living at Huancayo, Peru (10,170 feet), and at Morococha, Peru (14,900 feet), displayed changes primarily in the QRS, ST, and V waves during their adaptation to sea level (Lima, Peru, 500 feet). It is noted that the state of increased ventricular volume and hyperactivity which exists at high altitudes does not persist at sea level but is gradually modified.

Alzamora-Castro, V., G. Garrido-Lecca, and G. Battilana. Pulmonary edema of high altitude. Amer. J. Cardiol., 7:769-778 (1961). Twenty-seven cases of pulmonary edema of high altitude are reported. The disease occurred at an altitude above 3000 meters (9900 feet). Pulmonary edema of high altitude was observed in persons with normal hearts and often in young subjects. It occurred during the first trip, or on one or more of several trips, made to the higher altitude. Several patients were symptom-free in previous and subsequent trips to the same altitude. The disease was often observed in normal subjects adapted to the altitude, going back to the high lands after spending varying lengths of time at sea level. Respiratory infections were an aggravating or precipitating factor. Pulmonary edema of high altitude was usually preceded by symptoms which, as a rule, appeared shortly after arrival at the high elevation. The knowledge of the premonitory symptoms is important to prevent death. The treatment of choice is oxygen or, when possible, descent to lower altitudes or sea level. The cause of pulmonary edema of high altitude is obscure and the various possible mechanisms are briefly discussed.

Alzamora-Castro, V. Possible influence of high altitude on determination of various cardiac malformations; preliminary report. Revista Peruana Cardiol. 1:189-198 (July-Sept. 1952).

Alzamora-Castro, V., G. Battilana, R. Abuzattas, and S. Siola. Patent

ductus arteriosus and high altitude. Amer. J. Cardiol. 5(6):761-763 (June 1960). Patent ductus arteriosus is often found in patients born at high altitudes. The effect becomes manifest at altitudes over 3000 meters and is most evident at altitudes of over 4000 meters. It is presumed that mechanical factors affecting the pulmonary circulation as well as the lower oxygen tension may influence persistent patency of the ductus arteriosus. High altitude does not appear to be an etiologic factor in coarctation of the aorta.

Amassian, V.E. Effect of hypoxia and ischemia on cortical, thalamic, and midbrain reticular neurons. Abstract in Fed. Proc., 16 (1 part 1):3 (Mar. 1957). Spontaneous electrical activity and activity evoked by cat's forepaw, thalamic, or cortical stimulation was observed in records from medial lemniscus, midbrain reticular formation, medial and ventroposterior thalamic nuclei, internal capsule, somatosensory areas I and II and pyramidal tract. Spontaneous (including burst) activity in the cortex and medial thalamus practically disappeared before or when the arterial oxygen saturation fell below 10 percent. Early evoked somatosensory cortical responses, pyramidal responses, and evoked activity in single cortical neurons persisted many seconds. Activities of individual reticular neurons markedly differed in susceptibility to hypoxia, the activity disappearing either when cortical spontaneous activity disappeared or later. The latency of evoked discharge usually increased prior to loss of response.

Thus, transmission of short-delay evoked discharges within the cortex and is less sensitive to hypoxia than is the subcortical mechanism which drives cortical "spontaneous" activity.

Anderson, L. L., M. L. Willcox, J. Silliman, and S. Blount. Pulmonary physiology of normal individuals living at an altitude of one mile. J. Clin. Invest. 32:490-496 (1953). There are few known studies of pulmonary functions of normal, acclimated individuals living at a median altitude (1 mile). Therefore, the establishment of "normal" values for the various tests used in measuring pulmonary function was undertaken. Furthermore, the establishment of the effect of this median altitude upon the results of the tests is necessary for proper interpretation. Unfortunately, few studies of pulmonary function have been done at sea-level in a manner with which to compare these results. A significant increase in resting minute ventilation is established for one-mile altitude, and minute ventilation is increased during exercise. The increase in ventilation lowers carbon dioxide content and tension in the peripheral arterial blood below values obtained at sea level.

Anthony, A., E. Ackerman, and G. K. Strother. Effects of altitude acclimatization on rat myoglobin; changes in myoglobin content of skeletal and cardiac muscles. Amer. J. Physiol., 196(3):512-516 (Mar. 1959). Analyses were made of myoglobin content of rat skeletal and cardiac

muscle following continuous exposure to simulated altitudes of 18,000 feet for a 2- to 10-week period. Sixty rats were used. Acclimatization was associated with an increase in the myoglobin concentration of thigh, diaphragm, gastrocnemius, and heart muscles. Total myoglobin content, however, increased during acclimatization in cardiac muscle but not in the three skeletal muscles. This finding together with the body and muscle weight changes suggested that the increases in myoglobin concentration of skeletal muscles may be a reflection of a decreased muscle water content.

Apperly, F. L. Early blood changes during hyperventilation following residence at moderate altitudes. Amer. J. Physiol. 1:179-185 (April 1938).

Arellano, A. Cerebrospinal fluid at high altitudes; examination in case of Monge's disease. Neuro-Psequiat. Panam. Acta. 2:113-135 (1941).

Arellano, A. P. Circulatory speed at high altitude. Prensa Med. Argent. 31:50-58 (5 Jan. 1944).

Arellano, A. P. Intracranial pressure and high altitude; clinical considerations, especially psychoneurologic, of high plateaus; preliminary report. Revista Med. Exp. (Lima) 3:188-215 (July 1944).

Arias-Stella, J., and M. Saldana. The terminal portion of the pulmonary arterial tree in people native to high altitudes. Circulation 28(5):915-925 (1963). Hemodynamic studies have disclosed that people born and living at high altitudes present a mild degree of pulmonary-arterial hypertension and increased vascular resistance. Since the small muscular branches of

the pulmonary arterial tree are primarily concerned in determining vascular resistance: a study of their characteristics is included. Two series of autopsies were investigated—one from Cerro de Pasco at 14, 300 feet above sea level, and the other used as control, from Lima at sea level. Cases were arranged in two age groups: from 1 month to 2 years and from 6 to 76 years. Subjects of approximately matching ages were considered in both series. A more extensive muscularization of the peripheral pulmonary arterial branches at all ages, true hypertrophy of the proximal pulmonary arteries in adults, and evidence that some degree of vasoconstriction occurs in the distal arteries in younger ages were found in the high altitude series. The factors which probably give rise to these changes are discussed. It is believed that the results give an anatomical basis for understanding the genesis of high altitude pulmonary hypertension.

Arias-Stella, J., and H. Kruger. Pathology of high altitude pulmonary edema. Arch. Path. 76(2):147-157 (Aug. 1963). The pathological findings in two fatal cases of high-altitude pulmonary edema are described. The presence of alveolar and bronchiolar zonal edema accompanied by hyaline membranes was the most important lesion. In one case, recent thrombosis of the septal capillaries in both the small and medium-sized pulmonary arteries was another finding. The histochemical study of the hyaline membranes showed a structure similar to that found in the hyaline membrane disease of the newborn and in the placental "fibrinoid." The possible pathogenesis of the pulmonary edema and the significance of the presence of hyaline membranes are discussed.

Arias-Stella, J., and M. Saldana. The muscular pulmonary arteries in people native to high altitude. In Fifth Annual Conference on Research in Emphysema: Normal and Abnormal Pulmonary Circulation, Part 2, 1962. Med. Thoracalis; 19(5):484-493 (1962). A mild degree of pulmonary arterial hypertension, associated with increased vascular resistance, has been demonstrated in people born and living at high altitude. Since the small muscular branches of the pulmonary arterial tree are primarily concerned in determining vascular resistance, the study of their characteristics is necessary to understand the genesis and significance of high altitude pulmonary hypertension. Two autopsy series have been studied— one from people born and living from 11,300 to 14,300 feet above sea level, the other, used as control, from people born and living at sea level. The muscular pulmonary arteries were classified according to their topographic relation with the ramifications of the respiratory tree. Proximal arteries were defined as those located at the sides of terminal bronchioles; distal arteries as those situated at the level of alveolar ducts and alveolar septa. The ratio of the number of distal arteries to that of proximal arteries, the external diameter, the relation of internal to external diameter, the area of the media of proximal and distal arteries, and the total area of transversal arterial muscle at distal level per proximal artery were determined. A greater number of peripheral pulmonary arterial branches provided with a muscular media and the existence of more arterial muscle at the distal level, from one month of age onward, have been found in high altitude subjects. The results give an anatomic basis to understanding the histogenics of high altitude pulmonary hypertension.

Arias-Stella, J., and S. Recovarren. Right ventricular hypertrophy in native children living at high altitude. Amer. J. Path. 41:54-64 (July 1962). The ratio of left and right ventricular weights (LVW/RVW Hermann-Wilson index) was investigated in 70 infants and children born and living at sea level and in 59 like subjects from high altitudes (12,225 to 14,300 feet). In both, the cases were divided into 4 groups according to age: newborn or stillborn, 1 day to 3 months, 4 to 23 months, and 2 to 10 years. It was shown that at sea level the Hermann-Wilson index attained values corresponding to those characteristics of adults, beginning at the fourth month of life. In the high altitude group the ratio indicated a persistent right ventricular predominance which is normally present at birth, and ordinarily gives way in due course at sea level to left ventricular dominance. The apparent right ventricular hypertrophy persisted from the fourth month of life up to the maximum age investigated (10 years).

Arkad'evskii, A.S., A.P. Bruzhes, and E.A. Mukhamedova. On disturbances of muscle coordination in high mountain conditions. Biofizeka, 2(2):239-248. New York: Pergamon Press, 1957. Coordination disturbances were found in 75 percent of 60 subjects investigated on the second day of a stay at 4200 meters altitude (after 3 to 15 days of previous adaption to 2,200 meters). On the fifth day, slight residual effects persisted in 18 subjects studied. The disturbances consisted of overshooting the range in simple flexing movements, uneven speed of movement, and absence of correction in complex movements (in drawing lines, circles, and writing). The latency of the simple motor response was increased in 91 percent, and the maximum rate of motion simultaneously reduced in 61 percent of the subjects. Symptoms of excitation and discoordination in the higher cortical centers included euphoria, faulty associations, emotional disturbances, etc. The symptoms are interpreted as resulting from inhibition of the motor analyzer through negative induction from the excited higher cortical centers.

Armand-Delille, P.F. Altitude sojourn and secondary infection. Bull. Acad. Nat. Med. (Paris) 121:579-580 (21-28 Oct. 19·7).

Armstrong, H.G. and J.W. Heim. Effect of repeated daily exposures to anoxemia. J. Aviation Med. 9:92-96 (1938). It was previously shown that experimental animals exposed to an altitude pressure equivalent to 18,000 feet (1/2 atmosphere) for 4 hours daily exhibited an increasing tolerance to altitude for the first two weeks, followed by a progressively decreasing tolerance. The latter was accompanied by an increasing mortality rate due in certain cases to respiratory failure and in others to a paralysis of the lower half of the body. It was concluded that the primary cause of death in these cases was either a degeneration change in the central nervous system, the adrenal cortex, or both, although no direct evidence was presented to support this theory.

Asmussen, E., and M. Nielsen. The cardiac output in rest and work at low- and high-oxygen pressures. Acta Physiol. Scand. (Stockholm) 35(1):73-83 (1955). Cardiac output during 12- to 100-percent oxygen breathing was determined by the dye injection method. During low-oxygen breathing, an increase of 10 to 20 percent in cardiac output at rest and at work was associated with an increase in pulse rate and a slight decrease in stroke volume. High oxygen breathing caused a decrease in pulse rate of 4 to 8 percent but had no effect on cardiac output.

Aste-Salazar, H., and A. Hurtado. Affinity of hemoglobin for oxygen at sea level and at high altitudes. Amer. J. Physiol. 142:733-743 (Dec. 1944). The position of the oxygen dissociation curve has been determined in arterial blood obtained from (1) 17 healthy adult men living at sea level (2) 12 Indians, native residents of Morococha (Peru), at an altitude of 4540 meters (14,890 ft.). The same determination has been repeated in 12 subjects of the first group within the first two hours after arrival at the high altitude, and in 8 men of the second group within the first

two hours after arrival at sea level. The results have been compared with those obtained in previous investigations.

Astrand, P. O. Heart rate during muscular work in man exposed to prolonged hypoxia. J. Appl. Physiol. 13(1):75-80 (1958).

Astrand, P. O. The respiratory activity in man exposed to prolonged hypoxia. Acta Physiol. Scand. (Stockholm). 30(40):342-367 (1954). Two healthy subjects were exposed to simulated altitude in a low-pressure chamber for 66 to 115 hours (3000 or 4000 meters). On one subject, determination of pulmonary ventilation and alveolar pCO_2 etc., were done prior to, during, and after the period of acclimatization to hypoxia. The experiments comprised rest conditions and periods of work of varying grades of severity. On both subjects, the respiratory response to CO_2 mixtures was tested. By breathing oxygen, the hypoxic "drive" from the chemoreceptors was blocked and the effect of ventilation was examined. The results indicated that (1) the hypoxic "drive" occurring during acclimatization remained constant and of the same values as that seen in acute hypoxia; (2) in breathing air or oxygen, the pulmonary ventilation at any work level during prolonged exposure exceeded that seen in comparable experiments during acute exposure to altitude; and (3) following the period of prolonged hypoxia, the respiration was much more sensitive to CO_2 than was the case prior to the exposure to altitude. The effect of CO_2 +O_2 was more

pronounced than that of CO_2 + air.

Astrom, A. On the action of combined carbon dioxide excess and oxygen deficiency in the regulation of breathing. Acta Physiol. Scand. 27(98):61p(1952). Anesthetized dogs were exposed to inhalations of air containing excessive carbon dioxide and being deficient in oxygen. Arterial pH and O_2 saturation could be varied at will with the aid of a pneumothorax and of artificial respiration with different compositions of gas. Alveolar pCO_2 and pO_2 were measured simultaneously. The respiratory behavior was studied with the chemo-reflex mechanism intact or with exclusion of chemo-reflex influences. Respiration was found to be stimulated by CO_2. The stimulating effect of O_2 deficiency was found to be inversely proportional to the arterial pH. Breathing was stimulated markedly by intravenous injection of sodium cyanide at a low pH. A theory on the action of combined CO_2 excess and O_2 deficiency is evolved and practical applications of the findings are suggested.

Atmer. Studies on illness due to altitude. Acta. Aerophysiol. 1(3).50-52 (1934).

Aviado, D. M., and C. F. Schmidt. Physiologic bases for the treatment of pulmonary edema. J. Chron. Dis. 9:495-509 (1959).

Axelrod, D. R., and R. F. Pitts. Effects of hypoxia on renal tubular function. J. Appl. Physiol. 4(7):593-601 (1952). Hypoxia was induced

in two dogs and in two young men by inhalation of nitrogen-air mixtures while the oxygen content of the blood was recorded. Moderate hypoxia increased urinary flow; severe hypoxia, on the other hand, produced oliguria. The results showed however, that both in the man and the dog the renal tubular mechanisms for secretion of para-aminohippurate and for absorption of glucose are highly resistant to moderate or severe anoxia.

Aykut, R., M. Terzioglu, and M. Bilge. Energy exchange under basal conditions at rest and during exercise at 1850 meters altitude. Arch. Int. Physiol. 68:285-298 (Mar. 1960).

Aykut, R., M. Terziogly, and F. Ozer. Variations of the erythrocyte osmotic resistance and of the blood bilirubin level at an altitude of 1850 meters, Minerva Med. (Turin), 47(53):10-13 (4 July 1956).

Ten subjects staying at Uludag, Turkey(1850 meters of altitude), showed an 8-percent increase in erythrocyte values over those obtained at sea level. An increase in erythrocyte fragility and in blood bilirubin content was also observed, along with a decrease in erythrocytic osmotic resistance. These changes are probably related to the altitude-induced acceleration of hemolytic processes and the stimulation of erythropoietic activity.

Ayres, P. J., R. Hunter, and E. Williams. Aldosterone excretion and potassium retention in subjects living at high altitudes. Nature (London), 191(4763):78-80 (1 July 1961). Tests were made of a possible correlation between aldosterone and potassium levels in individuals subjected to a prolonged stay at altitudes above 15,000 feet. Urine samples were taken daily from 7 subjects (4 men and 3 women) during a 24-day stay at 14,300 feet on Mount Blanc. The results assume the validity of urinary aldosterone assay as an index of circulating aldosterone level. During ascent and at altitude circulating aldosterone and potassium initially tended to decrease, and after about 72 hours, to rise toward their sea level concentrations.

Ayzenberg, A. A., Y. S. Leschinskaya, and G. M. Robolotskaya. On the basic mechanisms compensating hypoxia in chronic circulatory insufficiency. AFSC N65-17791, Foreign Technology Div., Wright-Patterson AFB, Ohio. Certain consistent relationships in the compensation of hypoxia in chronic circulatory insufficiency are reported. In the initial stages of decompensation, the utilization of oxygen rises in response to the decrease in blood arriving at the tissue. In a later stage, hypoxia is compensated at the expense of reduced affinity of hemoglobin for oxygen, and the adjustment of metabolism with intensification of anaerobic processes. In patients suffering from heart defects with latent circulation insufficiency, the amount of circulating blood is lower than normal: it increases as decompensation develops. In the third stage of decompensation, the ability of the tissues to consume oxygen is lowered, histotoxic hypoxia develops, and resynthesis of lactic acid in the liver is suppressed.

B

Baciu, J., C. Oprisiu, and M. Dorostein. On the direct and reflex action of hypoxia in the nervous regulation of erythropoiesis. Medical Review 5(1):73 (1961). This work was carried out on dogs.

Badger, D. W., and N. Pace. Blood volume changes in dogs exposed to altitude. Physiologist 5(3):101 (Aug. 1962). Changes in red cell mass, plasma, and total blood volumes were compared in intact and splenectomized dogs living at 12,470 feet. Similar measurements were made in splenectomized dogs, whose aortic and carotid chemoreceptors had been ablated (glomectomized) to prevent respiratory response to hypoxia. All groups showed increased red cell mass. The intact and the splenectomized dogs reached 145 percent at sea level values, the latter more slowly. The glomectomized-splenectomized dogs increased to 250 percent, hematocrit values as high as 86 percent being observed. Plasma volume decreased within a few days in all groups, the intact dogs fell to 90 percent of sea level and returned by 60 days, the splenectomized decreased to 70 percent and recovered by 240 days, while the glomectomized decreased to 50 percent and had not recovered by 500 days. The erythropoietic response to hypoxia is slow in splenectomized dogs, although the same degree of increase in red cell mass as in intact dogs occurs eventually. On the other hand, the glomectomized-splenectomized dogs showed a far greater erythropoietic response to hypoxia than the other groups. It is apparent that the chemoreceptors are not needed for the erythropoietic response, but that the spleen may play

a role in erythropoiesis. Further, in the absence of hypoxic hyperventilation mediated by the glomi, the erythropoietic response is enhanced, with or without the presence of the spleen. Finally, the early decrease in plasma volume may be accounted for, at least in part, by activation of left atrial stretch receptors by hypoxia-induced, increased pulmonary venous pressures, with resultant decrease in ADH secretion.

Bahler, H. Influence of mountain climate on blood coagulation and blood platelet count. Schweiz Med. Wschr. 66:460-461 (9 May 1936).

Baicenko, I. P. Lactic acid content of blood at altitude of 4200 meters. Arbeitsphysiol. 6:373-375 (1933).

Baicenko, I. P., and A. N. Krestornikoff. Excretion of phosphorus in urine at altitude of 4200 meters. Arbeitsphysiol. 6:369-372 (1933).

Baird. B.. and S. F. Cook. Hypoxia and reproduction in Swiss mice. Amer. J. Physiol. 202(4) 611-615 (April 1962). Mice were maintained in closed decompression chambers continuously at simulated altitudes of 14, 200 and 16. 000 feet; intermittently, (6 hours per day) at 20, 000, 21, 500 and 25, 000 feet; and continuously at sea level with an atmosphere of 12-percent oxygen and 88-percent nitrogen. All animals were acclimatized before exposure. In all cases mating behavior was normal, and there was no functional impairment of male fertility. Impregnation was observed with all mated, adapted females in almost all experiments. Exceptions were considered due to early resorption of embryos. No significant effect of hypoxia was noted on implantation placentas, vascularization, or gestation time. Adverse effects of hypoxia were manifested primarily in resorption of fetuses when they had attained a critical size (about 7 mm.). The incidence of resorption is correlated directly with stress level, expressed as duration and intensity of hypoxia, and is considered to be contingent on the critically respiring mass of fetal tissue.

Baker, J. Possible allergic factor in altitude sickness. J. Lab. Clin. Med. 29:831-839 (Aug. 1944). Data are compiled from a random sampling of the records of private practice covering 500 youths (15 years of age and under) in Mexico City. Fifty percent of the youths were allergic; 167 had either severe hives, urticarial rashes, or eczema, and one hundred had gastrointestinal symptoms directly related to the ingestion of certain food. Evidence indicates that these symptoms are either milder or do not occur at all in these same individuals at lower altitudes. In individuals coming to Mexico City, a period of about three weeks is usually required in older children for the effect to accumulate and become manifest in symptoms. It is suggested that anoxia occurring at this altitude may result in a greater permeability of the gastrointestinal tract to offending substances. In view of the similarity in many cases to conditions found in mountain sickness, the possibility is suggested that similar factors may be contributing causes in such conditions and may be of interest in aviation medicine.

Balke, B., J.G. Wells, and J. P. Ellis. Effects of altitude acclimatization on work capacity. Abstract in Fed. Proc. 15(1^{I}):7 (March 1956). An attempt was made to measure the reduction of working capacity during acute and chronic exposure to altitude levels of 14,000 feet. A standardized test of gradually increased work load on a bicycle ergometer was applied at base level for controls, in a low pressure chamber and during a 6-week stay on Mt. Evans, Colorado. Comparable physical condition was achieved by a preceding physical training of 8-week duration. In all experiments the oxygen consumption at comparable work intensities remained practically unchanged. The pulmonary ventilation (BTPS) was almost doubled at altitude. Maximal ventilation observed was 122 liters per minute at base level but 170 liters per minute after some acclimatization on Mt. Evans. In the acute exposure to hypoxia the blood pressure was not altered. However, with previous acclimatization at 14,000 feet, systolic and diastolic pressure went up. The pulse rate exceeded the ground level values for some work intensities in the range of light and medium work load, though the pulse maxima were remarkably (11 to 14 percent) lower at altitude than at base level. On the average, 6 subjects in the performance tests in the low pressure chamber showed a reduction in work capacity of 27 percent.

Surprisingly, 6 weeks of acclimatization to an altitude of 14,000 feet were not sufficient to raise this performance level perceptibly. Immediately after return from the mountain, physical performance was improved above the controls. The maximal oxygen uptake was increased.

Balke, B., and J.G. Wells. Ceiling altitude tolerance following physical training and acclimatization. J. Aviation Med. 29(1):40-47 (Jan. 1958). The altitude tolerances of six subjects was tested in a low pressure chamber before and after physical conditioning training and after acclimatization to an altitude of 14,000 feet. The physical training resulted in an improvement of altitude tolerance of approximately 3,000 feet. Altitude acclimatization caused a further improvement of similar magnitude. Regular physical activity during the period of altitude acclimatization provided for faster and more effective adaptation. "Ceiling studies" were made with two subjects to investigate the combined effects of pressure-breathing tolerance and hypoxic tolerance at very high altitudes. In the control tests, subjects stayed at a simulated altitude of 50,000 feet for three minutes breathing 100-percent oxygen under a mask pressure of 30 mm.Hg. During this time, psychomotor performance deteriorated to 66 percent of normal. With altitude acclimatization in effect, the same subjects tolerated altitudes of 55,000 to 57,000 feet repeatedly for considerable length of time. Positive intrapulmonic pressures of 30 to 40 mm. Hg were tolerated for thirty minutes and longer without circulatory embarrassment. Intermittent daily exposure to simulated altitudes of 15,000 to 18,000 feet for one and one-half hours preserved the hypoxic tolerance gained by the natural altitude acclimatization.

Balke, B. Rate of gaseous nitrogen elimination during rest and work in relation to the occurrence of decompression sickness at high altitude. AF School of Aviation Med. Project No. 21-1201-0014, Report No. 6 Randolph AFB, Texas (Oct. 1954). Mild and severe exercises on the treadmill, with subjects breathing ambient air, did not increase the susceptibility for decompression sickness during subsequent ascents to high altitude. On the contrary there was a very slight trend toward an improved tolerance for high-altitude pains. Nitrogen elimination experiments on one subject at rest and at various levels of exercise were carried out. On the average, (in seven subjects) 640 cc. of tissue nitrogen were eliminated during 60 minutes of rest, 1580 cc. during 60 minutes of exercise on the treadmill at 2-percent grade, and 1050 cc. during 30 minutes of exercise at 5-percent inclination of the treadmill. In all instances the accumulated nitrogen elimination from blood and tissue, showed an approximately straight line relationship. In another experiment, it was noted that 60 minutes of preoxygenation during rest with a measured nitrogen loss of 640 cc. had practically the same effect as 30 minutes of denitrogenation with 400 cc. of nitrogen given off by the blood tissues. Two hours of preoxygenation at sitting rest almost doubled the tolerance time.

When oxygen breathing was continued during exercise for a period of 60 minutes, the same beneficial effect was obtained as after two hours of resting preoxygenation.

Balke, B., J.P. Ellis, and J.G. Wells. Adaptive responses to hyperventilation. J. Appl. Physiol. 12:269-277 (1958).

Ballard, R.W., Effects of hypoxia on shivering in man. Aerospace Med. 32:1143-1147 (Dec. 1961).

Barach, A.L., M. Eckman, and N. Molomut. Modification of resistance to anoxia, with especial reference to high altitude flying. Amer. J. Med. Sci. 202:336-341 (1941).

Barach, A.L. The treatment of anoxia in clinical medicine. Bull. N.Y. Acad. Med. 26:370-383 (1950).

Barach, A.L. The effects of oxygen deprivation on complex mental functions. J. Aviation Med. 8:197 (1938).

Barach, A.L., R. Brooks, M. Eckman, E. Gernsberg, A.E. Johnson. Appraisal of test of altitude tolerance. J. Aviation Med. 14:55-62 (April 1943). No evidence of physical or mental impairment was observed in any of the sixteen subjects at the end of an over-all period of two and a half to three months in which they were exposed to a simulated altitude of 15,000

feet for one and three quarter hours, two to four times a week. No decrease in the vital capacity of the lungs was found when correction was made for water vapor in the sixteen subjects studied repeatedly in this investigation and also in a group of other subjects tested at altitudes of 37,000 to 40,000 feet.

Baranski, S. Investigation on the incorporation of substances labeled by radioisotopes into the central nervous system in high altitude hypoxia. Rev. Med. Aero (Paris) 2:147-150 (Dec. 1961).

Barbashova, Z.I. Current concepts of the reorganization of cell chemism during acclimatization to hypoxia. AFSC N65-17811 Foreign Technology Div., Wright-Patterson AFB, Ohio (24 Nov. 1964). A study of the physical properties of muscle protein involved in contractile action was performed on the muscular tissue of rats. The viscosity of actomyosin changed, upon dilution at the same degree, whether the protein was isolated from normal animals or from those adapted to hypoxic conditions. This indicates that adaptation did not change the size or structure of the protein molecule. However, adenosine triphosphate (ATP) action reduced actomyosin viscosity because of the dissociation of protein into actin and myosin. Upon recovery, the actin and myosin molecules combined to form a molecule of actomyosin, which possessed a normal degree of viscosity. However, the recovery time was reduced after a hypoxic experience.

Barbashova, Z.I. Cellular level of adaption. In Hill, D.B. (ed.). Handbook of physiology, 4:37-54. Washington, D.C.: Amer. Physiol. Soc., 1964. Besides the well-known systems of changes, tissue or cellular adaptations are an important mechanism for the adjustment of organism to the action of unfavorable factors in the environment. In the case of an oxygen deficiency, there are two aspects: (1) the struggle for oxygen, and (2) adaptation to hypoxia. For different animals and sometimes for the same animals, when there are different degrees of hypoxic action, at times one and then the other mechanism or avenue of adaptation will be of primary importance. Some of the compensatory reactions, such as the extraordinary increase in the activity of the respiratory, circulatory, and blood-forming systems, indicate the incompleteness of acclimatization rather than its completeness. True adaptation of an organism to life in a changed environment is achieved mainly through metabolic and physiochemical reorganization at the tissue or cellular level, i.e., by means of tissue or cellular adaptation. The increase in resistance of tissue and cells is nonspecific, and this provides the basis for developing measures to increase the resistance of the human organism to the action of unfavorable environmental and industrial conditions, infectious diseases, etc.

Barbashova, Z.I. Effect of training in low pressure chamber on tolerance to oxygen hunger. Voen. Med. Sborn, 1:119-128 (1944).

Barbashova, Z.I. Effect of adaptation to hypoxia on the course of radiation disease. Kohlady Akademiimauk USSR (Moscow), 121(20):379-381 (Mar. 1955). The purpose of the study was to determine whether preliminary adaptation of animals to chronic oxygen deficiency had any preventive or ameliorating effect on radiation disease. When mice were used in the tests, adaptation to hypoxia was for six hours daily over a period of one month. Twenty-four hours after the last adaptation step, the mice were exposed to Co^{60} gamma ray irradiation as described. Recorded observations indicated that preliminary adaptation to hypoxia by the method lowered the mortality of the irradiated mice, slowed the rate of body weight loss, and mitigated the severity of the disease.

Barcroft, J. The respiratory functions of the blood: Lessons from high altitudes. London: Cambridge University Press, (1925).

Barcroft, J., et al. Observations upon the effects of high altitude on the physiological processes of the human body, carried out in the Peruvian Andes, chiefly at Cerro de Pasco. Proc. Roy. Soc. Biol. 211:351 (1943).

Barcroft, J. Alpinism. Lancet. 1:1277 (11 June 1921).

Bardalez-Vega, A. Some cases of acute pulmonary edema caused by severe altitude sickness. An. Fac. Med. (Lima) 38(2):232-243. Seven fatal and non-fatal cases are reported of acute pulmonary edema caused by severe altitude sickness in Peruvian natives living at high altitude. Subjects with pronounced tachycardia, decreased arterial pressure and embryocardia, and with reduced body efficiency responded to oxygen therapy in combination with digitalis. Subjects with less pronounced tachycardia, good arterial pressure, and less pronounced body efficiency responded to oxygen therapy alone.

Barer, A.S. Ionic shifts in the organism of the human and animals during hypoxic phenomena of various origins (subnormal barometric pressure, acceleration, vibration). AFSC N65-17809 Foreign Technology Div., Wright-Patterson AFB, Ohio, (24 Nov. 1964). Ion migration in the tissues of the human and animal organism was determined on the basis of potassium and sodium concentration in urine, saliva, and blood. The common response of the organism to various stresses (low pressure, acceleration and vibrations) was tissue hypoxia, primarily in the brain. At low altitudes, hypoxic hypoxia was noted. Acceleration caused circulatory hypoxia. Vibrations produced a combination of hemodynamic disturbances and tissue hypoxia. Migration of sodium and potassium ions in the interstitial fluid evidently depends upon the degree of permeability of the cell membranes in regard to these ions.

Barlett, F.H. On the variations of blood pressure during the breathing of rarefied air. Amer. J. Physiol. 10:149 (1903).

Barron, E.S.G. et al. Acute mountain sickness: The effect of ammonium chloride. J. Clin. Invest. 16:541-546 (1937).

Bartelheimer, H. Medical research on effects of high altitude. Med. Klin. 26:573-574 (1940).

Baur, F. Sun irradiance at different altitudes. Klin. Wschr. 1:2476-2477 (9 Dec. 1922).

Beard, E.F. Alterations in respiration, systemic circulation, and pulmonary circulation during moderate hypoxia in the dog. AF School of Aviation Med., Project 21-26-003, Report No. 1, Randolph AFB, Texas (Dec. 1951).

Beard, E.F., A.L.L. Bell, and T.W. Howell. Circulatory and respiratory responses to acute hypoxia in animals acclimated to altitude. J. Aviation Med. 24:494-507 (Dec. 1953). Ten mongrel dogs were kept almost continuously at a simulated altitude of 20,000 feet in a low-pressure chamber for seven to fifteen weeks and then used for acute hypoxia experiments performed under nembutol and morphine anesthesia according to a previously standardized technique using 8.5-percent oxygen in nitrogen to produce the acute hypoxic episode.

Becker, E.L., J.A. Schilling, and R.B. Harvey. Observations on renal function and electrolytes in the llama. AF School of Aviation Med., AD95-225, Randolph AFB, Texas (March 1955). Studies of the renal function were carried out on two llamas. Filtration rates were 30 to 37 cc. 100 gm. of kidney weight. Filtration fractions were 27 percent. The volume of distribution of inulin was approximately 14 percent of body weight. Autopsy findings and histologic studies were reported.

Becker, E.L., J.A. Shilling, and R.B. Harvey. Renal function in men acclimatized to an altitude of 15,000 feet. AF School of Aviation Med. AD 113530. Randolph AFB Texas. Studies of renal function were made on five normal men native to an altitude of 14,900 feet. Glomerular

filtration rates were determined by the constant infusion of inulin, and effective renal plasma flow was measured by the constant infusion of para-aminohippurate. All subjects showed a statistically significant decrease in filtration rate, and effective renal plasma and blood flow, with an increase in hematocrit and filtration fraction.

Becker, E. L., J. A. Schilling, and R. B. Harvey. Capillary vascularization in puppies born at a simulated altitude of 20, 000 feet. AF School of Aviation Med., AD 78-159, Randolph AFB, Texas (June 1955). Seven puppies born at an altitude of 20,000 feet were studied histologically for changes in capillary area. Significant increases in the capillary-tissue ratio were found in the brain, heart, and gastrocnemius. Other organs were examined, but were so engorged with blood that normal architecture and quantitative data were unobtainable. The possible significance of this increase ratio as an important step in acclimatization is discussed.

Becker, E. L., J. A. Shilling, and R. B. Harvey. Renal function in man acclimatized to high altitude. J. Appl. Physiol. 10(1):79-80 (Jan. 1957). Studies were made in the Andes at an altitude of 15, 000 feet on male natives who had lived continuously at high altitude. The results showed an 11-percent decrease in renal filtration rate, a 52-percent decrease in effective renal plasma flow, an 89-percent increase in filtration fraction and a 44-percent increase in hematocrit values as compared with individuals living near sea level. The acclimatized individuals represent a climato-

physiological variety of the human race different from sea-level dwellers.

Becker, E. L. Renal function in polycythemic dogs. J. Appl. Physiol. 10:75 (1957).

Becker, E. L., and B. J. Joseph. Observations of the inulin space in dogs during the process of adaptation to high altitude. AF School of Aviation Med., AD 113520, Randolph AFB, Texas (July 1956). The volume of distribution of inulin was studied in three dogs prior to exposure to a simulated altitude of 20,000 feet, and several observations over a period of 18 months were made after the dogs had become acclimated to the altitude. None of the values were significantly different from the control values.

Becker-Freyseng, H., H. H. Loeschike, U. Luft, and E. Opitz. Adaptation on Jungfraujoch respiration and acid-base equilibrium of blood during rest. Luftfahrtmedizin 7:160-179 (1942).

Becker-Freyseng, H., H. H. Loeschike, U. Luft, and E. Opitz. Adaptation on Jungfraujoch; respiratory volume and carbon dioxide system in acute oxygen deficiency before, during, and after altitude adaptation. Luftfahrt-Medizin 7:180-204 (1942).

Behnke, A. R. Physiologic effects of high altitude. U. S. Mar. Med. Bull., 39:163-178 (Apr. 1941).

Behnke, A. R. Physiological and medical aspects of aviation and deep sea diving. In advances in internal medicine. New York: Interscience Publishers Inc., 1946.

Behnke, A. R. Physiological effect of pressure changes with reference to otolaryngology. Trans. Amer. Acad. Ophthal. Otolaryng. 49:63-71 (Nov.-Dec. 1944).

Behnke, A. R. Decompression sickness incident to high altitude ascent (John Wyckoff lectures). Medicine, 24:381-402 (Dec. 1945).

Behnke, A. R. An approach to O_2 consumption in the "active protoplasmatic man". Fed. Proc. 11:11 (1952).

Behnke, A. R. Concepts derived from investigations pertaining to high altitude flight. J. A. M. A. 133:450 (1947). This paper enumerates some of the concepts and conclusions derived from extended research programs of the National Research Council, the Army, and the Navy, which are of interest to doctors of medicine, and it mentions some of the investigations currently under way which may have significant medical implication.

Beischer, D. E. The effect of simulated flight stresses on the conservation of serum cholesterol, phospholipid, and lipoprotein. Research Project No. NM001 107 102, Report No. 6, Naval School of Aviation Med., Pensacola, Fla. (Oct. 1955). Slight increases of cholesterol were caused by muscular exercise (a step-test and a treadmill run) and low temperature

(-10° C. for ten minutes). The stresses of low pressure (exposure of subjects in a low pressure chamber to simulated altitude of 15,000 feet for 20 minutes and 18,000 feet for 10 minutes in another series of experiments) and mental stress (simulated breakdown of the vacuum regulator), g-forces (4-g for ten seconds in human centrifuge), and hyperventilation had no influence on the serum cholesterol concentration. These slight and transient elevations of serum cholesterol have no pathological significance.

Beller, N.N. The role of interoceptors in the control of oxygen saturation of arterial blood. Biull. Eksp. Biol. Med. (Moskva) 43)6): 12-18 (June 1957). Studies were made of the oxygen saturation in arterial blood in animals during exposure to a simulated altitude of 7500 meters. Photoelectric oxygenometry was used for this study in rabbits and cats with denervation of the carotid sinus zones, as well as in controls. In the controls, the saturation diminished to 55-62 percent and increased somewhat after 8 to 10 minutes' exposure to altitude. In the experimental animals the diminution of oxygen saturation was more pronounced, reaching 40 to 50 percent and remaining within this range during the whole period of exposure. The experiment demonstrated that the dynamics and the degree of oxygen saturation of arterial blood in hypoxia depend on the function of the carotid sinus zones.

Beloshitskiy, P. V. and Lo Sin-mao. Change in the number of eosinophils under conditions of high altitude. AFSC N65-17828, Foreign Technology Div., Wright-Patterson AFB, Ohio (24 Nov. 1964). Experiments were conducted on guinea pigs in pressure chambers, and on guinea pigs, mice, and human subjects at altitudes of 2000 and 3500 meters. Low barometric pressure stimulated the activity of the hypophysis-adrenal system, as was indicated by the lowered eosinophil count of the peripheral blood. Injections of adrenocorticotrophic hormone under the same conditions led to a further drop in the eosinophil count which was beginning to normalize.

Benda, L., A. Locker, and E. Rissel. Cellular metabolism and inflammation: IV. Recovery respiration of the liver after hypoxia in vivo, Arch Ges. Exp. Med. (Berlin) 123(2):141-151 (1954). In continuation of previous research on the effects of decompression tissue respiration in the liver, this study investigates the effects of recovery in air. After cessation of decompression, an increase in cellular respiration was observed, which seems to depend on the suspension media. In a glucose-free bicarbonate-Ringer solution, the initial inhibition of respiration started quickly and returned to the normal values in the course of recovery. In a glucose-free phosphate buffer solution, the oxygen utilization also increased, while no changes were observed in a phosphate-Ringer solution. As to the mechanism of the observed metabolic reactions, it is hypothesized that endogenous (present) carbohydrates and exogenous

(available) carbohydrates compete with each other. The role of the reversible structural changes and of the inorganic phosphate is discussed.

Benson, O.O., Jr. The effect of decreased barometric pressure on the electrocardiogram. J. Aviation Med. 11:67 (1940).

Benzinger, T., R. Kaminski, and E. Opitz. Latent respiratory adaptation and its manifestation during additional oxygen deficiency. Luftfahrtmedizin 4:225-228 (1940).

Benzinger, T. Adaptation to altitude at 8000 meters acquired at 2000 meters above sea level. Luftfahrtmedizin 7:141-149 (1942).

Berendsohn, S. Hepatic function at high altitude. Arch. Intern. Med. (Chicago) 109:256-264 (Mar. 1962). Hepatic function studies were carried out in 30 residents of high altitude, by means of the determination of bilirubin, serum proteins, inorganic phosphorus, alkaline phosphatase, zinc, thymol, and cephalin-cholesterol flocculation, sulfobromophthalein excretion, and glutamic-pyruvic and glutamic-oxaloacetic transaminases. T... results were discussed and compared with findings in sea-level subjects. The probable causes of the abnormalities encountered in high-altitude subjects were discussed.

Berezovskivy, V.A. Energy indices to state of central nervous system in hypoxia. AFSC N65-17770, Foreign Technology Div., Wright-

Patterson AFB, Ohio. Determination of the oxygen saturation of the brain tissues in dogs by a polarographic method produced the following results: A temporary occlusion of one of the four major cervical arteries in dogs caused a decrease in the oxygen tension, and an increase in the temperature of the brain tissues. The radiation of impulses through the cerebral tissues, as a result of the hypoxic state of the central nervous system, produced an increase in the thermal conductivity of the brain tissues.

Berkovitch, E. M. Functional capacity of cardiovascular system among mountain guards of Donbass. Gig. Bezoposs Pat. Truda, 6(8)25-31 (1930).

Berlin, M. J., C. Reynafarje, and J. H. Lawrence. Red cell life span in the polycythemia. J. Appl. Physiol. 7(3):271-272 (1959). The red cell life span was found to be normal in Peruvian natives born and residing at an altitude exceeding 12,000 feet and having high-altitude polycythemia. Therefore, it may be assumed that altitude polycythemia is the result of an increase in the rate of red cell production rather than of a lengthening of the red cell life span.

Berlin, C., C. Reynafarje, and J. Lawrence. The influence of high altitude on erythropoietic activity; homeostatic mechanisms. Presented at the Tenth Annual Brookhaven Symposia in Biology, 1957.

Berne, R.M., J. Blackn , and T. Gardner. Hypoxemia and coronary blood flow. J. Clin. Invest. 36(7):1101-1106 (July 1957). In experiments on open-chest dogs and on fibrillating heart preparations, reduction of oxygen content of arterial blood produced increases in coronary blood flow only when coronary sinus oxygen levels fell below about 5.5-volumes percent. High perfusion pressures were employed in order to increase coronary flow to the extent that coronary sinus blood became relatively rich in oxygen. Under these conditions, it was possible to demonstrate that a moderate lowering of arterial oxygen content does not decrease coronary resistance by a direct action on the vessel walls. Coronary vasodilatation in hypoxemia appears to be related to myocardial hypoxia.

Berne, R.M. Cardiac nucleotides in hypoxia: possible role in regulation of blood flow. Amer. J. Physiol. 204(2):317-322 (1963). Experiments were performed on isolated cat hearts perfused with Tyrode's solution and intact hearts of open-chest dogs. Cardiac hypoxia resulted in a decrease in coronary vascular resistance and a release of significant amounts of inosine and hypoxanthine from the myocardium. From 3 to 27 times more inosine and hypoxanthine were released from the heart during myocardial hypoxia than were required to double the coronary blood flow when infused as adenosine into the left coro ry artery. A hypothesis is proposed for the metabolic regulation of coronary blood flow based on the assumption that with hypoxia, the nucleotide derivatives leave the myocardial cell as adenosine.

Bernthal, T., W. Greene, A. M. Revzin. Role of carotid chemoreceptors in hyponic cardiac acceleration. Proc. Soc. Exp. Biol. Med. 76:121-124 (1951). Though the increased heart rate which accompanies acute hypoxia is well known, the mechanism of its genesis is incompletely understood. Sands and De Graff and Wiggers have shown that it depends chiefly upon reduced toxic activity of the vagal cardio-inhibitory center and in lesser degree upon increased activity of the sympathetic cardio-accelerator center. However, the channels through which hypoxia operates when it alters the action of these centers have not been demonstrated.

Berry, L. J., and R. B. Mitchell. The influences of polycythemia produced at high altitude on resistance to infection: II. Effect of period of adaptation and period of recovery on resistance. AF School of Aviation Med., Project No. 21-35-005, Report No. 2, Randolph AFB, Texas (Oct. 1951).

Berry, L. J., and R. B. Mitchell. Influence of simulated altitude on resistance - susceptibility to S typhimurium infection in mice. Texas Rep. Biol. Med. 11:379-401 (1953).

Berry, L. J., C. Benzeville-Ferro, and C. Krumdieck-Boit. Metabolic studies of guinea pigs native to high Andes and the Peruvian coastal plain. Tissue of guinea pigs native to altitudes of 14,000 feet, or above, in the central Peruvian Andes and to the coastal plains of Peru were analyzed, with and without arsenite injections, for citric acid, pyruvic acid, and

alpha-ketoglutaric acid. Similar analyses were made on tissues of animals derived from each environment following periods of residence at the other experiment station. While differences were obtained, there was no uniform change, due, at least in part, to the large range of values found within groups. This variation in individual values may be attributed to the heterogeneity of the animals employed. It became evident, not only from tissue assays but also from mortality data, that the "downhill" stress may be as significant to a well-acclimatized altitude animal as the reverse change is for a "sea-level" animal. Manometric measurements on liver and kidney slices yielded lower $Q0_2$ values for kidney from altitude guinea pigs compared to sea-level guinea pigs. No differences were observed with liver slices derived from comparable animals. Sea-level animals at altitude for six weeks were more resistant to Salmonella typhimurium infection than altitude animals similarly infected.

Berry, L. T. Citric acid content of mouse tissues following altitude stress. AF School of Aviation Med. Report No. 57-152 Randolph AFB, Texas (Sept. 1957). Mice exposed to simulated altitude of 20,000 feet for three to four months show approximately the same percentage decrease in tissue citric acid as that previously reported for periods of three to six weeks. Altitude mice also show the same greater susceptibility to Salmonella typhimurium infection compared to controls as mice acclimatized for three to six weeks. The change in tissue citric acid associated with mice adapting to altitude could not be duplicated in animals given daily injection of 1 mg. cortisone acetate for two weeks prior to the assays. Nor was there a correlation between lowered blood sugar induced by 17 hours of inanition and reduced tissue citrate. This treatment, in contrast, was accompanied by elevated citric acid in all tissues.

Berry, L. J. Susceptibility to infection as influenced by acclimatization to altitude and Krebs cycle inhibitors and intermediates. J. Infect. Dis. 98:21-26 (1956).

Berry, L. J. Tissue citric acid content and susceptibility to infection in mice acclimatizing to and recovering from altitude. AF School of Aviation Med., AD 113832, Randolph AFB, Texas (Aug. 1956). Citric acid concentration of blood, liver, spleen, kidney, duodenum, and heart of mice acclimatizing to a simulated altitude of 20, 000 feet progressively declined to a level 30 percent below control values (heart 20 percent) after 3 weeks in decompression chambers and remained unaltered during 3 additional weeks of exposure. Animals kept in the chamber for 3 weeks and returning to normal atmospheric pressures showed no change in citrate concentration after 5 days of recovery. After 10 days of recovery, liver and spleen had normal amounts of citric acid, but remaining specimens were normal only after 14 days. Susceptibility to Salmonella typhimurium infection was

greatest when the citric acid concentration was significantly lower than that of the control group. When citrate was normal, susceptibility was normal.

Berry, L. J. Citric and lactic acid content of tissues and susceptibility to infection as influenced by acclimatization to altitude. AF School of Aviation Med., AD 78160, Randolph AFB, Texas (July 1955). During the acclimatization of mice to simulated altitude, the citric acid concentration of several organs was significantly lowered. The lactic acid concentration was unaltered in the same tissues. The susceptibility of mice exposed to altitude for three weeks and then infected intraperitoneally with either Salmonella typhimurium or pneumococci was compared to the susceptibility of infected normal mice following injections of Kreb's cycle inhibitors or intermediates. Altitude mice kept at ground level only in the presence of injections of oxaloacetate, citrate, and saline, the latter serving as controls for the other substances injected. Higher mortality to pneumococci occurred with malonate and saline in altitude mice as compared with normal mice. Uninfected altitude mice are more susceptible than normal mice to injections of arsenite and malonate.

Berry, L. J. Effect of acclimatization to altitude on susceptibility of mice to influenza A virus infection. Proc. Soc. Exp. Biol. Med. 88(4):543-548 (Apr. 1955). Mice acclimatized to a simulated altitude of about 20,000 feet for three weeks are more resistant to infection with

influenza A virus than normal mice, mice similarly acclimatized but given 3 weeks of recovery at normal pressures prior to infection, and mice made anemic by blood loss, the latter three groups showing no significant differences in susceptibility. Acclimatized mice maintained at altitude for the postinfection period are more resistant than those maintained at atmospheric pressures. These results are attributed to a metabolic disturbance which accompanies acclimatization to altitude and reduces the animal's capacity for virus synthesis.

Berry, L. J. Altitude stress; its effect on tissue citrate and salmonellosis in mice. Proc. Soc. Exp. Biol. Med. 96(1):246-249 (Oct. 1957).

Berry, L. J., and D. S. Smythe. Carbohydrate metabolism in normal- and altitude-exposed mice following arsenite poisoning. Amer. J. Physiol. 197(1):37-40 (July 1959).

Berry, L. J. and D. S. Smythe. Effect of cortisone on protein loss and carbohydrate gain in normal and simulated altitude-exposed mice. Amer. J. Physiol. 199:407-411 (Sept. 1960). After injection of cortisone in fasted mice, protein catabolism and carbohydrate synthesis were equal; but in fasted altitude-exposed (simulated 20, 000 feet for 3 to 5 weeks), these were less carbohydrate than protein. In fed mice of both groups a balance between protein loss and carbohydrate increase was observed after cortisone administration, but the absolute quantities were less in altitude-exposed animals. Fasted altitude-exposed mice excreted more urinary nitrogen than controls. Administration of bacterial endotoxin to the hypoxic group decreased the urinary nitrogen to normal levels. Altitude-exposed mice were significantly more susceptible to endotoxin than normal mice. Glutamic-oxaloacetic and glutamic-pyruvic transaminases were lower in the livers of altitude-exposed mice than in normal animals. These enzymes were also lower four weeks after adrenalectomy.

Beutler, F., and R. Stampfle. Changes in conductivity of blood and plasma in high mountain climate. Helvet. Physiol. Pharmacol. Acta 6:688-698 (1948).

Beyne, J. Disturbances of human organism caused by high altitude flight. Ann. Physiol. 10:331-358 (1934).

Bezuglyy, V.P. Oxygen starvation in pathological conditions of the liver. AFSC N65-17802. Foreign Technology Div., Wright Paterson AFB, Ohio. Gas composition . arterial and venous blood, oxyhemoglobin dissociation, and carbonic acid fixation is reported for patients with Botkin's disease. Changes in the gas composition of the blood, oxyhemoglobin dissociation, and carbon dioxide fixation occur in acute virus hepatitis. Oxygen saturation of the arterial blood decreased; oxygen content of the venous blood decreased; oxygen difference in the arterial venous blood increased. Hemoglobin affinity for oxygen decreased. In addition to an increase in the oxygen saturation percentage of the arterial blood, the oxyhemoglobin dissociation tended to normalize during recovery. Carbon dioxide transport was also disrupted and an accumulation of this gas formed in the tissues. The presence of tissue oxygen starvation during the disease makes it necessary to take special measures to prevent hypoxia.

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Blasius, W. Relation between hemoglobin content and altitude tolerance. F. Kreislaufforsch 37:581-594 (Oct. 1948).

Blasius, W., and E. Bauereisen. New method of improving human altitude tolerance in decompression chamber. Luftfahrtmedizin 6:67 (1943) and Bull. War. Med. 3:410 (March 1943).

Blood, F.R., et al. Relationship between hypoxia oxygen consumption and body temperature. Amer. J. Physiol. 156:62-66 (Jan.-Mar. 1949). The oxygen consumption and body temperature of normal, and thyroxin- and thiouracil-treated rats were determined at three environmental temperatures and five altitude levels between 5,280 and 40.000 feet. The data obtained

indicates: oxygen availability becomes a limiting factor in oxygen consumption only at altitudes approaching 40,000 feet in normal rats but at much lower altitude in animals whose metabolism has been stimulated by cold or by thyroxin; although a reduced consumption of oxygen is in general accompanied by a fall in body temperature, instances occurred where the two factors apparently varied independently of each other.

Blood, F.R., R.V. Elliott, and F.E. D'Amour. The physiology of the rat in extreme anoxia. Amer. J. Physiol. 146:319 (1946). In this study, data concerning a number of respiratory and circulatory functions were obtained in the rat, at elevations of 5,280 and 40,000 feet, in order to obtain some knowledge of the adaptations made by this highly resistant animal to extreme anoxia.

Blood, F.R., D.L. Smith, and F.E. D'Amour. Cardiac output in the rat at normal and high altitudes. Amer. J. Physiol. 163:268-271 (Nov. 1950). A method has been developed for the determination of cardiac output in the rat at normal and high altitude using the Fick principle. The cardiac output in the rat at Denver's altitude (5280 feet) was found to be 46.5 ml/min. The cardiac output decreases when an animal is taken from normal to high altitude; the relative magnitude of decrease appears to have some relationship to the development of gas embolism. A close correlation exists between cardiac output at high altitude and the occurrence of gas embolism.

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Blumenfeld. Distribution of surface pressure of atmosphere on external surfaces of body and on internal surfaces (lung) of man at various altitudes. Schweiz. Med. Wsthr. 66:1089-1091 (7 Nov. 1936).

Bodansky, O., and C.D. Hindley. Effect of methemoglobin on visual threshold at sea level, at high altitudes, and after exercise. J. Clin. Invest. 25:717-722 (Sept. 1946). Cancellations of methemoglobin up to 30 percent were induced without showing any definitely significant effect upon the rod threshold in dark adaptation either at sea level or at simulated high altitudes of 12,000 feet and 18,000 feet. Short bouts of severe exercise lower the rod threshold immediately after exercise in the methemoglobinemic individual, but not in the normal individual. However, 5 to 10 minutes after exercise, the threshold rises above the normal to the same extent in both methemoglobinemic and nonmethemoglobinemic individuals. The above findings are discussed with reference to oxygen unloading in tissue and to the effect of exercise on the acid-base balance.

Bogatskaya, L.N., N.S. Verkhratskiy, L.V. Costyuk, and V.V. Frol'kis. On the age-connected peculiarities of the reaction of the heart to hypoxia. AFSC N65-17764, Foreign Technology Div., Wright-Patterson AFB, Ohio.

Myocardial hypoxia is one of the most commonly encountered pathogenic mechanisms that disturbs the function of the heart. In experiments with rabbits, it was observed that as the organism aged there was a change in the proportions between anaerobic and aerobic phases of respiration. Further, the heart of the aged is more sensitive to pathological processes that result in hypoxia of the myocardium. The age-connected peculiarities of the heart to hypoxia were shown by experiments with aged and young rabbits in which the development of myocardial infarct was observed by tying off the circumflex branch of the left coronary artery. A large number of fibrillations of the heart was noted in aged subjects.

Bogdonova, L. V. On the adaptation of lower vertebrates to hypoxia. AFSC N65-17753, Foreign Technology Div., Wright-Patterson AFB, Ohio. In order to study the adaptation of lower vertebrates to hypoxia, experiments were conducted at altitudes of 2000, 3000, 4000, and 5000 meters on frogs, turtles, and racers. Of 12 turtles, 4 showed a certain speedup in the respiratory movements, while 2 showed slower and another showed very slight respiration. In the racers (Zamenis gemonensis), residence at an altitude of 2100 meters produced no change in their respiration. When the altitude was increased to 3000 meters, an increase in the oxygen capacity of the blood rather than a respiratory reaction was observed at altitudes of 2150 and 3000 meters.

Boles-Carenini, B., and V. Cima. Study of the behavior of color sensitivity (Rayleigh's Equation) by Nagel's anomaloscope during reduced oxygen

supply to the eye. Riv. Med. Aero. 15(4):527-542 (1952).

Test for color sensitivity (with Nagel's anomaloscope) were carried out on three groups of subjects. Twenty young subjects, Group I, inhaled a mixture poor in O_2, corresponding to an altitude of 6000 meters. In Group II comprising 30 subjects, compression of the eyeball induced local ocular hypoxia. Group III, about 30 subjects, serving as controls, first inhaled pure O_2 and then had pressure applied on the eyeball. Results of the tests were as follows: general hypoxia induced abnormalities of color perception and aggravated existing abnormalities; the inhalation of O_2 improved color sensitivity under normal atmospheric conditions; pressure upon the eyeball induced anomaly of the red-green chromatic perception; and compression of the eyeball and inhalation of O_2 neutralized their mutually antagonistic effects.

Bona, G.B. Effects of one-sided diet on people living in high altitudes. Med. del. Lavoro. 23:22 (Jan. 1931).

Bonnardel, R., and W. Liberson. Physiology of human work in high altitudes. C.R. Acad. Sci. 194:1265-1267 (11 April 1932).

Boothby, W.M., W.R. Lovelace, and O.O. Benson. High altitude and its effect on the human body. J. of the Aeronautical Sciences. 7:524 (1939).

Boothby, W.M., U.C. Luft, and O.O. Benson. Gaseous nitrogen elimination: experiments when breathing oxygen at rest and at work with comments on dysbarism. J. Aviation Med. 23(2):141-158, 176 (1952). The authors measured the nitrogen elimination from the tissues of subjects breathing oxygen from successive rebreathing bags. The pulmonary nitrogen was first washed out by six maximal expirations and inspirations of pure oxygen without rebreathing. When the elimination tissue nitrogen is plotted against time on a log-log graph, a straight line results. Physical work (walking on treadmill) speeds up the nitrogen elimination as compared to rest (sitting). Formulae are derived expressing the amount and rate of nitrogen elimination as functions of time and of constants denoting individual variations and physiological state (work). The rate of nitrogen elimination from the various parts of the body differs; the first to be eliminated is the pulmonary nitrogen, followed by that contained in the intrathoracic organs, and finally that of other organs. No evidence has been found that the skin takes up nitrogen from the surrounding air, but these experiments are not conclusive—a sufficient degree of denitrogenation before ascent to altitude prevents dysbarism (decompression sickness).

Boothby, W. M., W. R. Forelace, O. O. Benson, and A. F. Strehler. Volume and partial pressures of respiratory gases at altitude. AF School of Aviation Med., Project No. 21-2301-0003:39-49 (Sept. 1954).

Boothby, W. M. Effects of high altitudes on the composition of alveolar air: introductory remarks. Proc. Staff Med. Mayo Clin. 20:209-213 (27 June 1945). With the assurance that the composition of alveolar air reflects to a first approximation the gas tension of arterial blood, one is largely justified in using the oxygen and carbon dioxide pressures in alveolar air as an index of the adequacy of the oxygen provided by the gas inhaled under particular environmental conditions. The collection of extensive data showing the respiratory responses to high altitude are greatly facilitated when it is no longer necessary to draw samples of arterial blood but only to expire forcibly into a tube.

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Borsky, I., M. Hajzokova, and M. Hubac. Changes of certain blood values in workers of the cable car system in Tabanska Lomnica. Pracov Lek. 12:426-430 (Oct. 1960).

Borth, R., and R.S. Mach. Steroid excretion and blood status during a mountain tour and a stay at medium altitude. Acta Endocr. 6:310 (1951). Four healthy subjects were investigated during a stay in a mountain town at 1850 meters of altitude and during time-control periods at 400 meters for changes in the 17-ketosteroids excretion, in corticosteroid excretion, and in the blood. The stay at 1850 meters caused a slight decrease of 17-ketosteroids excretion, a very small increase of corticosteroid excretion, an increase of erythrocytes and hemoglobin, marked variation of the absolute eosinophil count and a slight increase of their ratio (percent of differential leukocyte count), a decrease of the segmented neutrophils, and an increase of the lymphocytes.

Bourdillon, T. D. The use of oxygen apparatus by acclimatized men. Proc. Roy. Soc. (London) 143(910):24-32 (Dec. 1954). During the British Cho Oyu Expedition in 1952 and the Everest Expedition in 1953, observations were made regarding the use of oxygen equipment by men fully acclimatized to high altitudes. Descriptions are given for an open-circuit apparatus, closed-circuit apparatus, and sleeping set. A detailed account of the use and effect of oxygen apparatus during the Everest expedition is included. These expeditions have provided further evidence of the lasting benefit of previous acclimatization to high altitude which is so marked as to suggest some definite physiological changes. Both types of climbing oxygen apparatus were found very successful and it was felt that they permitted the climbers to cover longer distances in one day. The sleeping set proved very valuable in keeping high altitude deterioration within reasonable limits.

Boutwell, J.H., C.J. Farmer, and A.C. Ivy. Studies on acid-base balance before and during exposure to altitude, or to hypoxia and hyperventilation. J. Appl. Physiol. 2:391 (1950).

Bowen, W.J., and J.H. Eads. Effects of 18,000 feet simulated altitude on the myoglobin content of dogs. Amer. J. Physiol. 159:77-82. Two experiments studied the effects of six-hour daily exposures to simulated altitude on the myoglobin content of muscle in seven dogs. The anterior trapezius of the one side was analyzed before the initial exposure, and the muscle of the other side was analyzed after the final exposure. The myoglobin content of five muscles in the exposed dogs was compared with the content of the same muscles in six unexposed dogs. In all exposed dogs, the hemoglobin content increased markedly during the exposure but the average myoglobin content of the trapezius decreased slightly. Also, the myoblobin content of the other five muscles was less in the exposed dogs than in those unexposed.

Boycott, A.E., and J.S. Haldane. The effects of low-atmospheric pressures on respiration. J. Physiol. 37:355 (1908).

Braginskii, V.M., and M.M. Mirzoev. Effect of vitamins on the functions of the adrenal cortex in residents of the Pamir at 3700 meters altitude. In Makarchenko, A.F. (ed.). Oxygen Deficiency, pp. 461-464. Kiev: Akademiia Nauk Ukrainskoi, SSSR (1963). A determination of the 24-hour output of 17-ketosteroids was conducted on a group of residents of the Pamir at an altitude of 3700 meters as an indicator of the functional state of the adrenal cortex. Large doses of vitamins (50 mg. riboflavin, 100 mg. vitamin E, and 500 mcg) given daily increased the functional state of the adrenal cortex. However, daily doses of 30 mg. folic acid reduced adrenal cortex activity.

Brandan, R. A. Physiologic action of mountain climate in Cordoba, Argentina. Acta Argent, Fisiol. Fisiopat. 1:151-217 (1950).

Branscomt, B. V., and G. W. Wright. Effects of controlled low oxygen breathing upon exchange of respiratory gases in humans. Fed. Proc. 11(1[I]):16 (1952). The gas exchange in a human subject was measured continuously by the open-circuit method throughout the following consecutive phases of an experiment: (1) breathing air without controlled breathing pattern (20 min.), (2) breathing air (pO_2, 148-153 mm. Hg) with controlled breathing pattern (30 minutes), (3) breathing an oxygen-nitrogen mixture (pO_2, 105-115 mm. Hg) with controlled breathing pattern (60 minutes), and (4) breathing air with or without controlled breathing pattern (20 minutes). The CO_2 output remained constant through all periods. The oxygen uptake decreased markedly during period (3) to 10-40 percent of the control level.

Brazier, M. A. B. Studies on the physiology of flight, effect of anoxia on the electroencephalogram of psychoneurotic and normal adults. Arch. Neurol. (Chicago). 56:725-729 (1946).

Brendel, W. Adaptation of respiration, hemoglobin, body temperature, and circulation during an extended sojourn at high altitudes (Himalayas). Pflueger. Arch. Ges. Physiol. (Berlin) 263(2):227-252 (1956). Periodic measurements were made of the circulatory and respiratory functions of mountain climbers before and during an

extended Himalayan expedition. The transition from sea level to altitudes of 4000 to 7000 meters produced increases in respiratory volume, hemoglobin level, and blood pressure and a decrease in heart rate. Rectal temperatures declined in several subjects in correlation with relatively great increases in respiratory volume. The response of blood pressure and heart rate to the performance of a standard exercise at altitude was decreased by altitude acclimatization from that observed at sea level or at altitude prior to acclimatization.

Brener Cukier, J. Adrenal stimu ·tion in acute anoxia expressed in the variation of circulating eosinophils. An. Fac. Med. (Lima) 37(1):100-133 (1954). Adrenal function, as determined by the circulatory eosinophil count in persons subjected to acute anoxia living in high altitudes was compared with that of persons living at sea level. In the majority of anoxic persons a decrease in the number of circulating eosinophils was observed which was caused by adrenal stimulation. The majority of subjects with acute altitude sickness demonstrated more intense eosinopenia, in comparison to normal subjects. This indicates a more intense adrenal stimulation in subjects with altitude sickness, a response related to the intensity of the stimulus. The number of circulating eosinophils in 25 normal young fasting subjects varied between 70 to 372 per cubic millimeter at sea level. Eosinophils vary spontaneously in a 4-hour interval (8-9 a.m. to 12-1 p.m.), demonstrating a decrease.

Brooks, R.A., and J.L. Reeves. Influence of intermittent exposure to simulated altitude on organ histology in rats. AF School of Aviation Med. 60-81:1-8, Randolph AFB. Texas (19 Sept. 1960). A study of histologic changes in kidney, lung, liver, spleen, testis, brain, hypophysis, and striated muscle was made as part of an investigation of male Sprague-Hawley rats exposed four hours a day to 18,000 feet (equivalent) altitude. Few histologic changes were found which could be attributed to the altitude exposure. Hemosiderin was deposited in the renal tubules, but not in the liver. In most instances, less lymphatic tissue was found in the lungs of the altitude-exposed rats than in the lungs of controls. Fatty changes were not found in the organs of the exposed animals. Morphologically, there was no indication that intermittent exposure to 18,000-foot altitude caused significant pathologic alterations of the organs examined.

Brooks, C.M., M.T. Ang, and R.T. VanDam. An experimental study of some effects of hypoxia and respiratory acidosis on the mammalian heart. Jap. Heart J. (Tokyo) 3(1) 34-35 (Jan. 1962). In the *in situ* dog heart, hypoxia induced by 10-percent O_2 ventilation produced an initial slight shortening of conduction time and a definite lowering of the threshold. Ultimately, a depression of ventricular excitability and A-V conduction occurred. Rapid induction of respiratory acidosis, induced by 2 to 12.8 percent CO_2 mixtures, caused an early temporary depression of ventricular diastolic excitement. When induction of acidosis was slow, this depression was slight or absent, and an enhancement was observed in some cases. The depressant actions of hypoxia and acidosis appeared to be counteracted, to some degree, by a compensatory mechanism. The state of ventricular excitability and A-V conduction at any instant seems to depend on the balance between two opposed mechanisms. The total refractory period of the ventricular myocardium was only slightly prolonged by hypoxia and respiratory acidosis, but more markedly by ammonium chloride administration. After termination of hypoxia, ventricular diastolic excitability returned readily to a normal level, whereas A-V conduction time remained lengthened for a much longer period. Refractoriness also was not very stable. The A-V conducting system appears less resistant to the depressant effect of hypoxia and acidosis than the ventricular myocardium.

Brown, A. L., G. F. Vawter, and J. P. Marbarger. Temperature changes in human subjects during exposure to lowered oxygen tension in a cool environment. Aviation Med. 456-463 (October 1952). Healthy male human subjects exposed to either 30 mm. Hg (18,000 feet) without supplementary oxygen or breathing gas mixtures low in oxygen, and in a cool environment showed significant changes in heart rate and in systolic and diastolic blood pressures when compared to the responses elicited during exposure to a cool environment uncomplicated by anoxia. Skin and rectal temperature in these subjects were not significantly different, during exposure to hypoxia in a cool environment, than those observed during exposure to the same environment in the presence of adequate oxygen. The response in humans to exposure to a cool environment does not appear to be significantly altered by a reduced partial pressure of oxygen in the inspired air: This is contrary to opinions often expressed by flying personnel. The individual variations observed in these experiments warrant further studies on responses of capillary beds to environmental changes produced by combined effects of temperature and reduced barometric pressure.

Brown, J. L., J. Hill, and R. Burke. Effect of hypoxia on the human electroretinogram. Amer. J. Ophthal. 44(1):57-67 (July 1957). Hypoxia was induced in two subjects by having them breathe, at atmospheric pressure, oxygen-nitrogen mixtures which contained lower percentages of oxygen than that found in normal air. The amplitude of retinographic response to stimulation by red light was reduced by more than five percent while subjects breathed a mixture containing 9-percent oxygen. This mixture is equivalent to the atomsphere at an altitude of 20,000 feet.

Brown, J. H. U. Failure of the respiratory responses to low oxygen tensions. J. Aviation Med. 27(5):460-461 (Oct. 1956). Three cases are noted of persons who failed to respond to low oxygen tension with the usual respiratory reflexes attributed to the carotid body. These cases occurred

during an experiment conducted in a course of medical physiology to illustrate the carotid body response to low-oxygen tension.

Brown, H. N. Oxygen at what altitude? Inhalation Therapy 7(5): 10-12, 20-21 (Oct. 1962). The first evidence of hypoxia occurs at 5000 feet in the form of diminished night vision. Oxygen should be used while flying above 5000 feet at night. At 10,000 feet there is definite but undetectable hypoxia requiring the use of oxygen. At this altitude, the blood oxygen saturation level is 90 percent, compared to 95 percent at sea level. At 14,000 feet, when the oxygen saturation drops to 84 percent, the symptoms are as follows: diminishing vision, hand tremor, clouding of thought and memory, and judgement errors. At 16,000 feet, when the blood oxygen saturation level drops to 77 percent, the individual becomes disoriented, belligerent or euphoric, and completely irrational. Between 18,000 and 20,000 feet, neurocirculatory collapse or primary shock occurs, and collapse or even death is possible. An outline of oxygen equipment is presented and an oxygen dissociation charts is included.

Brown, R. H. "Empty field" myopia and viability of distant objects at high altitudes. Amer. J. Psychol. 70:376-385 (1957). Previous studies by others have "shown...that the nearsightedness induced by the (empty) visual field at high altitude may account in part for difficulties in detecting planes." The present study shows that this condition cannot be designed into equipment and indicates "the possibility of improvement in air-to-air search by personnel selection."

Brown, G.A. Nervous system dysfunction in adaptation to high altitude and postflight reactions. War Med. 1:157-161 (Mar. 1945).

Bruce, C.G. The assault on Mount Everest, p. 339 London: Edward Arnold and Company, 1933.

Bruner, H., D. Joxy, and K.E. Klein. Hypoxia as a stressor. Aerospace Med. 32:1009-1018 (Mar. 1961). On the basis of altitude tests included in earlier general aptitude examinations for pilots, a new method was developed, which better meets the requirements of stress conditions imposed on pilots today by revealing their general stress resistance. This method makes use of a new apparatus by which the efficiency behavior under the influence of a nonspecific stressor (defined oxygen deficiency) is objectively and reproducibly registered. Method and evaluation processes are discussed in detail.

Bryantseva, L.A. Certain data on the anatomical physiological characteristics of the organism of children born and raised in the high mountains. AFSC, N65-17759 Foreign Technology Div., Wright-Patterson AFB, Ohio. A survey of children, between the ages of 7 and 16, who were born at an altitude

of 2050 meters and remained permanent residents of the location, disclosed certain deviations from the normal physiological and morphological characteristics. The average height was less than normal, but the weight was within the normal limits. The thoracic girth and the vital capacity were increased. The respiration rate was normal; however, the minute respiratory volume was increased. The pulse rate was lower than normal, and a small group developed a slight bradycardia. The electrocardiogram showed, in general, low amplitudes, with the exception of the T wave which in many instances was of greater amplitude than normal. The blood flow rate was low. In 40 percent of the cases the capillary resistance was low. The high pulmonary ventilation and the low blood flow rate may provide better oxygen saturation of the blood in the pulmonary circulation. However, it is possible that the tissue requirements for oxygen are lower at high altitudes.

Buchner, F. Structural changes produced by general oxygen deficiency, especially in altitude sickness. Luftfahrtmedizin 6:281(1942).

Buchner, F. Pathogenic effects of general oxygen deficiency, especially in altitude sickness and death. Klin. Wschr. 21:721 (15 Aug. 1942); Abstract in Bull. War Med. 3:409-410 (Mar. 1943).

Buess, H. Angelo Mosso, pioneer of mountain physiology. Schweiz. Med.

Wschr. 763:502 (June 1946).

Bugard. The limits of human resistance in high altitude and depth. Atomes (Paris 7(77):255-260, 280 (1952). The physiological implications of high altitude are outlined briefly, and data concerning aeroembolism, explosive decompression and resistance to anoxia, and acceleration are tabulated. A graphic representation is given of the physical characteristics of the atmosphere of high altitude.

Buhler, A. Circulation studies in high mountain areas. Praxis (Bern) 46(50):1131-1133 (12 Dec. 1957).

Buhlmann, A. and J.R. Hofstetter. Exercise tests at median altitudes. Helvet. Physiol. Pharmacol. Acta 9:222-226 (1951).

Buhlmann, A., S.J. Wang, H.Wirz, and F. Verzar. Erythrocyte count in median altitude. Schweiz. Med. Wschr. 81:80-82 (27 Jan.1951).

Buianov, P.V. Changes in respiration, blood circulation and peripheral blood in man after a prolonged stay at high altitudes. Voennomed. Zh. 3:25-29 (Mar. 1960).

Bullard, Robert, W. Effects of hypoxia on shivering in man. Aerospace Med. 32(12):1143-1147 (Dec. 1961). When human subjects after 30 minutes of exposure to 5°C breathed 10 percent O_2, an increase in shivering activity and O_2 consumption occurred. The increase usually subsided after 15 minutes. The recovery periods following the hypoxic breathing were often characterized by greatly decreased shivering activity. Both heart rate and pulmonary ventilation rates were higher in hypoxic cold-exposed subjects than in hypoxic subjects in a 30°C environment. It is hypothesized that the shivering increase is a release phenomenon.

Burchell, H.B., and E.H. Wood. Demonstration of differential effects on pulmonary and systemic arterial pressure induced by breathing low-oxygen mixtures. Fed. Proc. 10:21 (Mar. 1951).

Burr, H.S., and R.B. Livingston. Effect of hypoxia and hypercapnia on standing potential of man. Fed. Proc. 11(1^I):21 (1952). Measurements of "standing potentials" (DC potential of the body), which vary with increasing anoxia and hypercapnia, were made on 18 medical students in an attempt to activate a signal warning mechanism against anoxia. Change in potential began at 15,000 feet. Withdrawal of oxygen at 26,000 feet caused a marked shift in potential prior to collapse. Similar alterations in standing potentials were observed in subjects after breathing of increasing amounts of CO_2.

Burrill, M.W., and A. C. Ivy. Excretion of neutral 17-ketosteroids in humans subjects repeatedly exposed to hypoxia under conditions of simulated high altitude. J. Appl. Physiol. 2:437 (1950).

Burrill, M. W., S. Freeman, and A. C. Ivy. Sodium, potassium and chloride excretion of human subjects exposed to simulated altitude of 18,000 feet. J. Biol. Chem. 157:297-302 (Jan. 1945). Exposure to reduced pressure, under the conditions of the experiment caused a temporary rise in the excretion of sodium potassium and chloride. Following exposure, the excretion of these electrolytes was compensatorily reduced, so that total excretion during the 24-hour period was not altered. A temporary rise in urine volume was also found to accompany exposure.

C

Cabieres, Molina, F. Cardiovascular vegetative system in relation to life in high altitudes. An. Fac. Med. (Lima) 29: 5-124 (1946).

Caccia, A.R., F.O. Debarnot, L.G. Munilla, and I.T. Russi. Cataract and altitude. Sem. Med. (B. Aire) 115:751-763 (5 Nov. 1959) and 115:691-702 (29 Oct. 59).

Cain, S.M. Cerebral excess lactate production during hyperventilation of anesthetized dogs. SAM-TDR-62-109. AF School of Aerospace Med., Aerospace Medical Division, Brooks AFB, Texas. Eight anesthetized, curarized dogs were ventilated to alveolar pCO_2, pO_2, pH, hemoglobin saturation, lactic acid, and pyruvic acid. The vasoconstriction of the cerebral vessels was clearly demonstrated by the increased arterio-venous difference in hemoglobin saturation which increased on the average from 26 to 45 and to 48 percent during the two periods of hyperventilation. Sagittal sinus pO_2 declined from 41mm. Hg during the control to 29 and 25mm. Hg with hyperventilation. Calculation of cerebral "excess lactate" production from the measurements of lactic

and pyruvic acids showed no significant increase with hyperventilation. The conclusion was made, with reservation, that cerebral oxygenation during even severe hyperventilation was sufficient to maintain normal oxidative metabolism.

Cain, S.M. and J.E. Dunn II. Increase of arterial oxygen tension at altitude by carbonic anhydrase inhibition. AF School of Aerospace Med., Task No. 775801, Aerospace Medical Division, Brooks AFB, Texas (Sept. 1964). Unanesthetized dogs were injected intravenously with 10 mg./kg. per 12 hours of the carbonic anhydrase inhibitor, acetazolamide, before exposure to a simulated altitude of 21,000 feet (P_B = 335mm. Hg). Arterial blood samples were drawn frequently from a Teflon T-cannula surgically placed in a carotid artery one or two days before the experiment. Arterial pO_2, pCO_2, pH, and lactic and pyruvic acid concentrations were measured. In comparison with untreated dogs, arterial pO_2 at altitude was 9mm. Hg higher, on the average, in treated animals. No physiologically significant accumulation of excess lactate was found. The conclusion was made that carbonic anhydrase inhibition did offer measurable protection, with respect to arterial pO_2 against altitude hypoxia and that this protection was achieved with much smaller doses of drug than had been used by other investigators.

Cain, S.M. and J.E. Dunn II. Transient arterial lactic acid changes in unanesthetized dogs at 21,000 feet. Amer. J. Physiol. 206:1437-1440 (1964). After a 3-hour control period at ground level, unanesthetized dogs were exposed for 8 hours to 21,000 feet simulated altitude (P_B = 335mm. Hg). Arterial blood samples were drawn frequently from a Teflon T-cannula surgically placed in a carotid artery one or two days prior to the experiment. Lactic and pyruvic acid concentrations, pCO_2, pO_2, and pH were measured. At altitude, the average arterial pO_2 was 32mm. Hg, pCO_2 was 24mm. Hg and pH was 7.50mm. Hg. All control values fell in normal ranges. Although the magnitude of changes differed among animals, arterial lactic acid reached a peak value with the first two hours at altitude, gradually declining thereafter and, in most animals, closely approached the control value during the eighth hour at altitude. Excess lactate changed in a similar manner, with no concomitant relief of arterial hypoxia and hypocapnia. The decline in lactic acid remains unexplained.

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Campbell, J. A. Living at very high altitudes and maintenance of normal health. Lancet 1:370-373 (15 Feb. 1930).

Campos, Rey de Castro, and B. Iglesias. Mechanisms of material acclimatizations: Preliminary report on anatomic studies at high altitudes. School of Aviation Med., AD126831, Randolph AFB, Texas (June 1956). Preliminary postmortem pathological studies are reported of specimens from 30 Andean natives acclimatized to altitudes of about 4000 meters. Most of the natives died in accidents. The organs investigated include the lungs, trachea, bronchi, heart, liver, spleen, kidneys. striated muscle, ovaries, testes, and, in several cases, brain and adrenal glands. All alterations found are considered to be related to the environmental hypoxic factor, the most constant changes being congestion and dilation of blood capillaries and sinusoids.

Campos, J. Rey de Castro, and B. Iglesias. Anatomical and pathological data on 49 normal persons native to and residents of high altitudes (3,700 to 5,000 meters) who died accidentally. Rev. Lat. Amer. Pat. 1(2):109-130 (July 1957).

Cannon, J.L. The estimation of the cerebral blood flow from the arterial carbon dioxide tension: II. Applications in Aviation Medicine. Naval School of Aviation Medicine, Project No. NM001 059.06.08, Pensacola, Florida. Data found in the literature permit the estimation of the cerebral blood flow, the cerebral arteriovenous oxygen difference and the cerebral venous oxygen tension at any altitude. This information has been placed on a pCO_2 - pO_2 diagram to make it conveniently usable. From the presentation, a more satisfactory explanation for "oxygen paradox" is evolved.

Cannon, W.B. and R.G. Hoskins. The effects of asphyxia, hyperpnea and sensory stimulation on adrenal secretion. Amer. J. Physiol. 29:274-279 (1911).

Capdehnuat, E.L. Interesting clinical facts observed on plateaus of Bolivia. Piensa Med. Argent, 24:2443-2449 (22 Dec. 1937).

Capdehnuat, E.L. Estudios sobre la biologia del hombre de la altitud. Ministeria de Justicia e Instruction Publica, (B. Air.) (1937).

Carlson, A.J. Life at High Altitudes. Nature (London) 148:774-776 (27 Dec. 1941). The chain of events involved in acclimatization (as contrasted with short-run compensation) has been seen to involve a series of reactions: Lactic acid in the blood remains unchanged while at rest. After the first few hours of adjustment, the saturation of oxygen in the arteries attains a constant level. Lung ventilation is maintained at an increased rate. Arterial blood, after initial alkalinity, eventually assumes its usual reaction. Both free and combined carbon dioxide in the blood are reduced, but the ratio between them, which governs the respiratory center is eventually restored to its usual value.

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effects of exposure to a simulated altitude of 20,000 feet in a decompression chamber before and after a single intravenous injection of a carbonic anhydrase inhibitor were observed in five trained unanesthetized dogs. Pulmonary ventilation, alveolar gas exchange composition and pH, gas tensions, and CO_2 content of the arterial blood were observed. The drug, in a single dose of 100 mg./kg, produced the following effect when combined with acute hypoxia: (1) hyperventilation was greater than that resulting from hypoxia alone; (2) a smaller decrement in the alveolar and arterial pO_2 followed ascent to altitude; (3) a subsequent rise in alveolar and arterial pO_2 if administered after attaining altitude; (4) a greater decrement in alveolar pCO_2 following ascent to 20,000 feet; (5) a higher arterial blood H-ion concentration than that associated with hypoxia alone; and (6) a greater decrease in plasma CO_2 content during adjustment to acute hypoxia. Theoretical calculations were made which indicated that the pulmonary capillary blood has a higher pH and a lower plasma CO_2 content than the peripheral arterial blood after administration of the inhibitor.

Cassiano, O. Maximum respiratory work in adaptation to high altitude. Boll. Soc. Ital. Biol. Sper. 39:206-209 (28 Feb. 1963).

Cassinelli, C. M. Dextrose, lactic acid, and pyruvic acid in blood at sea level and at high altitude. An. Fac. Med. (Lima) 32:1-28 (1949).

Catacora, G. M. Renal calculosis in autochthonus inhabitant of Bolivian Plateau. Rev. Argent. de Urol. 15:405-408 (Jan. -Dec. 1964).

Cerretelli, P. Some aspects of the respiratory function in man acclimatized to high altitudes. Int. Z. Angew. Physiol. 18 (5):386-391 (1961).. This study investigates the effect of a 60-day period of acclimatization at 5000 meters altitude on some respiratory parameters, i. e. vital capacity, inspiratory reserve volume, tidal air, maximal exercise ventilation, the resting ventilation, and the composition of the alveolar gases at rest. The most striking results, besides the expected fall in PA_{CO_2}, were a decrease in vital capacity of 9.84 ± 4.34 and 12.54 ± 3.80 percent after 30 days and 60 days of acclimatization respectively and a still greater reduction of 21.84 percent in maximum pulmonary ventilation during exercise. The possible causes of these phenomena are discussed.

Cerretelli, P., and R. Margaria. Maximum oxygen consumption at altitude. Inf. Z. Angew. Physiol. 18:460-464 (1961). On 11 subjects, members of an Himalayan expedition, observations have been collected on maximum oxygen consumption (VO_2) max. and some respiratory and circulatory characteristics at sea level and at altitude after a 60 day acclimatization period. The most striking changes as compared with sea level values (=1.00) are: (1) a fall in the maximum exercise ventilation to about 0.78, (2) a fall in the energetic efficiency of respiration to about 0.55, (3) a fall of the vital capacity to about 0.87, (4) a fall of the PA_{CO_2} to 0.55, (5) an increase of blood haemoglobin to 1.32, (6) a decrease of the VO_2 max. to about 0.44, and (7) a decrease of the maximum heart rate to about 0.80.

Cerretelli, P. The behavior of the vital capacity under the effect of prolonged stay at very high altitude (Himalayas). Boll. Soc. Ital. Biol. Sper. 35:1922-1923 (31 Dec. 1959).

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Chand. D. et al. Heart and lung function studies in tropical high mountainous conditions; body performances in the Simla mountains (Himalayas); viewpoints for prevention of heart diseases in high altitudes. München. Med. Wschr. 101(7):265-270 (13 Feb. 1959).

Chang, M. C., and L. Fernandez-Cano. Effects of short changes in environmental and low-atmospheric pressure on the ovulation of rats. Amer. J. Physiol. 196:653-655 (1959).

Chapin, J. L. Ventilatory response to oxygen breathing of individuals acclimatized to altitude. J. Aviation Med. 25:500-503 (1954). The ventilatory responses to high-oxygen inhalations of nine healthy individuals acclimatized at Denver, Colorado were measured. There was a marked depression of ventilation during the first minute of oxygen breathing. The next ten minutes of oxygen breathing showed a return of ventilation toward normal values. The first five minutes of recovery in air showed an overshoot in ventilation.

Chapin, J. L. Comparison of rebreathing and breath-holding breaking-point curves at 5300 feet. Fed. Proc. 14(1^{I}):27 (Mar. 1955). A comparison was made of breath holding and rebreathing breaking-point curves at altitude with 15 to 50 percent inspired oxygen. Rebreathing in all cases produced higher alveolar CO_2 and lower O_2 values than did breath holding. Rebreathing gas (high in oxygen) resulted in subjective sensations of marked vasomotor disturbance with sweating. Rebreathing 100 percent O_2 produced an axillary temperature increase of 0.5 percent, an increase in ventialtion to 66 percent of maximum

breathing capacity, a heart rate increase of 41 percent, increase in systolic and diastolic blood pressures of 44 and 16 mm. Hg respectively.

Chenykayeva, Ye. Yu. Investigation of oxidative metabolism enzymes (succinoxidase and cytochrome) in the cerebral cortex and myelencephalon in hypoxia-acclimated rates. AFSC N65-17813, Foreign Technology Div., Wright-Patterson AFB, Ohio. Determinations of succino-oxidase and cytochrome oxidase levels in the cardiac muscle, brain cortex, and medulla were conducted in albino rats subject to hypoxia during several generations. Each new generation showed a tendency toward an increase in anaerobic glycolysis and changes in the cytochrome system, characteristic of a higher tolerance to hypoxia. The hemoglobin content and the number of erythrocytes, as well as the level of carbon-hydrase activity, remained elevated. A combination of these factors led to greater tolerance to hypoxia. However, after the seventeenth generation, the hemoglobin content normalized. The hypoxia adaptation mechanism was transferred to the tissue system, that is, the cytochrome system, primarily in the medulla.

Cherkasskiy, L. P. On the influence of hypoxia caused by decrease in atmospheric pressure on cardiac activity of animals that have undergone pneumonectomy. AFSC N65-17783, Foreign Technology Div., Wright Patterson AFB, Ohio. Experimentation on the influence of hypoxia on rabbits in an altitude chamber at various points in time after removal of a lung is reported. Removal of a lung reduces the organism's reserve capabilities for adaptation to hypoxic conditions. Nevertheless, it was found that the disturbed functions were compensated to a degree after the operation so that experimental animals with one lung were, in many cases, capable of resisting rather considerable degrees of artifically induced hypoxia.

Cheymol, J. Hyperthermal agents and hypoxia. C.R. Soc. Biol. (Paris) 149(3-4):338-343 (Feb. 1955). The effectiveness of the hyperthermal agents, antigonococci vaccine (acting on the thermoregulatory mechanism), dinitrophenol (acting by increasing metabolic activity), and β-tetrahydronaphthylamine (combined action), in counteracting hypoxic hypothermia was studied. Rabbits were exposed to simulated altitudes of 5000, 7000, or 9000 meters for 7 hours, at a normal ambient temperature during the period of exposure, and demonstrated that while β-tetrahydronaphthylamine had no effect, the antigonococcic vaccine and, to a lesser extent, dinitrophenol, quantitatively counteracted the hypoxic hypothermia.

Cheymol, J., and C. Levassart. Tissue hydration and resistance to hypoxia. Bull. Soc. Chim. Biol. (Paris) 38(2-3): 547-555 (1956). Hydration of adult rats by intraesophageal injection of large quantities of water or by intraperitoneal injections of isotonic glucose solution produced a significant increase in survival rate during exposure to a simulated altitude of 11,000 meters. It is suggested that hypoxia causes an accumulation of metabolic waste and an elevation of intracellular osmotic pressure, and that intracellular hydration allows the maintenance of an isotonic state. The increased resistance of young animals to hypoxia is attributed to their greater hydration.

Cheymol, J., and R. Henry. Polyglobulia; question of difference according to age of rabbit. Bull. Soc. Chim. Biol. (Paris) 29:86-88 (Jan. - Mar. 1947).

Chiatellino, A. Relation of changes in blood to function of spleen. Bull. Soc. Ital. Biol. Sper. 4:7-9 (Jan. 1929).

Chiatellino, A. Effects of splenectomy on changes in blood due to mountain climate. Arch. Sci. Biol. 15:407-432 (Mar. 1930).

Chiatellino, A. High altitude effects upon blood corpuscle resistance. Arch. Fisiol. 25:310-324 (July - Sept. 1927).

Childs, S.B., J. Hamlin, and Y. Henderson. Possible value of inhalation of carbon dioxide in climbing great altitudes. Nature (London) 135:457-458, (23 Mar. 1935).

Chiodi, H. Blood picture at high altitude. J. Appl. Physiol. 2:431 (1949).

Chiodi, H. Oxygen affinity of the hemoglobin of high altitude mammals. Acta Physiol. Lat. Amer. 12:208-209 (1962). The oxyhemoglobin dissociation curve of the pooled blood of two chinchilla (Chinchilla brevicandata, a native high-altitude rodent) was determined. The half-saturation point corresponded to an oxygen tension (pO_2) of 24 mm. Hg; compared to a pO_2 of 34 mm. Hg. in the rabbit, and 18 mm. Hg. in the alpaca (Lama paro). These findings agree with those of Hall, Dill, and Guzman-Barron (1936) who studied the high-altitude camelids, the vicũna and llama, and two species of birds, the huallata, or Bolivian goose, and the South American ostrich. High-altitude representatives of the species studied thus far have a blood hemoglobin with a greater affinity for oxygen than that of their sea-level relatives. A table is included listing the oxygen affinity of equilibrated blood of chinchilla, rabbit, and alpaca.

Chiodi, H., and Carlos Pozzi. Hematic values in residents at altitude between 1260 and 4515 meters above sea level. Acta Physiol. Lat. Amer. 11(2) 51-59 (1961). The number of red cells, hemoglobin, and hematocrit values increased with altitude beginning at 2078 meters. The mean corpuscular hemoglobin and the mean corpuscular volume decreased progressively between 1260 and 4515 meters while no significant changes were observed in the mean corpuscular hemoglobin concentration.

Chiodi, H. Respiration adaptations to chronic high-altitude hypoxia. J. Appl. Physiol. 10(1):81-87 (Jan. 1957). Adult males who had either lived for long continuous periods at high altitudes or those who had been lowlanders and newly arrived at high altitude were studied at altitudes of 3990 and 4515 meters. At both altitudes, resting pulmonary ventilation was significantly lower in the long-term residents than in the newcomers but not as low as in the average sea dweller. Changes in pCO_2, alveolar ventilation and oxygen ventilatory equivalent were in accordance with those in total ventilation; therefore, hyperventilation was greater in the newcomers. Oxygen breathing depressed the average ventilation in the newcomers, and respiratory response to inhaled CO_2 was also greater. Response to inhaled CO_2 in long-term

residents was equal to or less than that of sea-level subjects. Hemoglobin-oxygen affinity and arterial pH of the long-term residents were found to be within the normal sea-level ranges. It appears that it is necessary for subjects to acclimatize to altitude for longer periods than previously suggested.

Chiodi, H. Respiratory regulation at high altitudes; Regulation of human respiration (J.S.Haldane Centenary Symposium). Oxford: Blackwell Scientific Publishers, 1961.

Chiodi, H. Mountain sickness of cerebral form. Possible etio-pathogenic mechanism. An. Fac. Med. (Lima) 43:437-447 (1960).

Chiriboga, J. Incidence and characteristics of mal del pinto in eastern Andes of Peru. Rev. Argent. Dermatosif 34:116-130 (June 1950).

Chirico, M., and G. Benda. On the extrarenal clearance of sodium thiosulfate in conditions of induced hypoxemia. Biol. Lat. (Milan) 9(3):433-440 (July - Sept. 1956). The extrarenal clearance of sodium thiosulfate was studied in ten dogs breathing a mixture of ten percent oxygen in nitrogen. A more or less evident decrease in the clearance rate was found, probably related to the reduced metabolic activity in the liver induced by hypoxia.

Christensen, W.R., and A.B. Hastings. Acid-base balance of rats exposed to reduced barometric pressures. J. Aviation Med. 20:221 (1949).

Clamann, H.G., and H. Hartmann. Cooling of aortic blood during inhalation of cold air and its effect on oxygen binding capacity and on altitude tolerance. Luftfahrtmedizin 1:292-300 (1937).

Clark, R.T., and A.B. Otis. Comparative studies on acclimatizations of mice to carbon monoxide and to low oxygen. Amer. J. Physiol. 169(2):285-294 (1952). Mice acclimatized to prolonged exposure to gradually increasing concentrations of CO survived oxygen deficiency (simulated altitude) for longer periods than did untreated controls. Similarly, mice acclimatized to low-oxygen concentrations survived exposure to CO (0.25 percent) longer than untreated animals. Blood studies of the mice acclimatized to CO revealed a higher CO_2 capacity of the plasma and a lower CO_2 capacity of the whole blood as compared to the controls. In the mice acclimatized to low O_2, the CO_2 capacity was reduced for both plasma and whole blood (as has also been observed in humans living at high altitudes). Both the CO and anoxic

groups showed a considerable loss of weight which was regained upon return to normal environment. The rate of oxygen consumption was about the same in the experimental groups and controls.

Clark, R.T., H.J. Chinn, J.P. Ellis, W.E. Pawel, and D. Criscuolo. Tissue respiratory studies during chronic altitude and cold exposure. Air Force School of Aviation Med., Project No. 21-1201-0009, Report No. 3, Randolph AFB, Texas (Dec. 1953). A slight, but significant, decrease in oxygen uptake was found for liver slices from rats chronically exposed to altitude using glycerophosphate as the substrate. Under similar experimental conditions, the respiration of liver slices from cold-exposed rats was markedly increased. Liver slices from the exercised, altitude-exposed rats had a significantly lower Q_{O_2} than did slices from control animals similarly exercised. No significant difference was evident between these groups when the liver slice was allowed to respire in air of 12.5-percent oxygen. Cyclophorase activity of liver and kidney was determined in cold-exposed rats, and of liver, kidney, diaphragm, heart, soleus muscle, gastrocnemius muscle, and brain of altitude-exposed animals. Only the activity of the diaphragm was significantly higher after exposure.

Clark, R.T., D. Criscuolo, and C.K. Couilson. Effects of 20,000 feet simulated altitude on myoglobin content of animals with and without exercise. Fed. Proc. 11(1[1]):25 (1952). Gastrocnemius and diaphragm muscles of hamsters acclimatized for six weeks to a simulated altitude of 20,000 feet without exercise were analyzed for myoglobin content. A lower myoglobin content was found in the acclimatized animals than in the ground controls. Hemoglobin content had risen to 18.8 mg. (per gm. wet tissue) compared to 12.0 mg. in the controls. In another experiment, 100 male rats were divided into 4 groups: Group I was exposed to a simulated altitude of 20,000 feet and exercised at that altitude for 20 minutes; Group II was exposed to altitude without exercise: Group III was exercised at ground level; Group IV stayed at ground level without exercise. Myoglobin content of the heart muscle and that of the gastrocnemius of altitude-exercised animals increased during acclimatization about 20 and 54 percent, respectively, over the myoglobin content in the animals exercised at ground level. Myoglobin levels in groups II and IV were lower than in other groups.

Clark, R. I., D. Criscuolo, G. Grey, G. Hataway, and H. M. Sweeney. Mechanisms of adaptation to chronic hypoxia within the tissues. Proceedings of Nineteenth International Physiological Congress.

Montreal, Canada, 1953. Adult rats were divided into four groups: groups I and II were exposed to a simulated altitude of 18,000 feet; groups III and IV were ground controls. Groups I and III were exercised each day on a treadmill. Twelve animals from each group were sacrificed every seven days for a period of 70 days in order to study the myoglobin, enzymes, and degree of capillarization of various tissues. In addition to these groups, another series of weanling rats were completely adjusted to a simulated altitude of 18,000 feet. Twenty-six of this series were sacrificed after 120 days at altitude. Myoglobin values for heart, diaphragm, and gastrocnemius muscles showed 40- to 50-percent increase over the 70-day exposure period in groups I and II as compared with groups III and IV. Exercise produced a moderate additive effect. The most significant increase was between the twenty-eighth and thirty-fifth days. After the thirty-fifth day, a gradual decline was noted. Completely acclimatized rats showed the same myoglobin values as sea-level controls. The heart and Tibialis anticus were studied histologically for capillary response to high altitude. Heart and Tibialis anticus muscles showed 39- and 30-percent increase in number of functioning capillaries respectively. The surface area for heart muscle capillaries was 90 percent greater in acclimatized than in control animals and 300 percent greater for Tibialis anticus. The results achieved by this method indicate a decrease in diffusion gradient of O_2 to the tissues by both an increase in number and a dilation of capillaries. Q_{O_2} values on liver slices using glycerophosphate as a substrate were 11.4 for acclimatized animals and 11.0 for control animals.

Clark, R. T., I. Christlut, M. Sanmaico, Diay-Perey, and J. F. Hammann Jr. Relationship of hypoxia to archythmia and cardiac condition hemorrhage. Circulation 27(4 Pt. 2):742-747 (1963). The relationship between hypoxia, arrhythmia, and hemorrhage of the conduction system was studied in an experimental laboratory by making several different groups of rats and dogs hypoxic, and by the histological examination of the area of the atrio-ventricular node and bundle of His in sections obtained from the hearts of these animals. Sixty-one percent of rats aged two weeks or older developed arrhythmias and had hemorrhage. Ten baby rats presented no changes when submitted to the same type of experiment. Hemorrhage was present in only 40 percent of asphyxiated dogs and in 40 percent of dogs that were made hypoxic during cardiopulmonary bypass; 75 percent of dogs which underwent total mitral valve replacement and expired in acute pulmonary edema 3 to 10 days postoperatively presented a similar type of lesion. In most

cases, the administration of oxygen sufficed to reverse the E C G changes back to normal. Hypoxia is suggested as the primary cause for these changes, on the basis of previous clinical and experimental work and the information collected from these experiments. The importance of a possible species difference was suggested when attempts were made to correlate the results in rats, dogs, and humans.

Clinton, M. Jr., G. W. Thorn, and U. D. Davenport. Studies on altitude tolerance. Bul'. J. Hopkins Hosp. 79:70 (1946).

Cockett, A. T. K. Effect of altitude on formation of urinary bladder calculi in male rats. Aerospace Med. 34(2):108-110 (February 1963). A method is presented for the formation of vesical calculi in male rats at simulated altitude. Weight of urinary bladder calculi formed experimentally in male rats at low barometric pressure without hypoxia (18,000 feet) is not significantly greater than calculi formed experimentally in rats at ground level. The significance of dehydration, rather than altitude in flying personnel, is mentioned. The possibility of urinary calculi as a result of extended space flight must await studies performed under altitudes and prolonged weightless conditions.

Cohn, E. W., and F. E. D'Amoru. Effect of high altitude and cobalt on growth and polycythemia in rats. Amer. J. Physiol. 166:394-399 (Aug. 1951).

Colehour, J. K. Hypoxia: A high-altitude hazard. Aircraft Owners and Pilots Association, 2(8):22, 48-49 (Aug. 1959). The effect of hypoxia on mental, sensory, and metabolic processes and muscular performance upon ascent to altitude are reviewed. Although adaptation to altitude up to 18,000 feet is possible, it is considered impractical in aviation due to the time factor involved. The detrimental effects of hypoxia are intensified by the presence of noxious gases and carbon-monoxide carrying power of red blood cells, because of the reduction in the normal oxygen. Carbon monoxide not only from exhaust fume leakage into the aircraft but also from smoking can hasten the incapacitation of the pilot by hypoxia. Oxygen is recommended for pilots on night flights above 5,000 feet, all flights between 10,000 and 12,000 feet altitude, and all jet flights.

Colehour, J. K., H. Borsook, and A. Graybiel. The effect of hypoxia on the serum iron and the unsaturated iron-binding capacity of serum in rats. Naval School of Aviation Medicine, AD 144099, Pensacola, Fla. 16 July 1957. The changes in concentration of unbound iron binding capacity (UIBC) and bound iron (BI) in rat serum under hypoxic stress are measured. After one day at altitude, UIBC increases acutely and is followed by a decrease in BI on the second day. Reticulcytes reach peak values at four days while hematocrits were 30 percent above starting values at the end of ten days. Twelve days after return to sea level, iron values were back to normal.

Comfort, E., and J. W. Wilson. Some factors affecting the time of consciousness at high altitudes. Air Force Technical Report No. 5970 (Nov. 1959).

Comroe, J.H., P.R. Dripps, and M. Deming. Oxygen toxicity: The effect of inhalation of high concentrations of oxygen for twenty-four hours on normal men at sea level and at a simulated altitude of 18,000 feet. J.A.M.A. 128:710 (1945). One-hundred percent oxygen administered to a large group of normal men continuously for twenty-four hours produced substernal distress in 82 percent. Vital capacity was usually decreased significantly. Signs of nose and throat irritation were common. Control subjects breathing room air through the same apparatus did not experience the symptons. Intermittence (up to fifteen minutes rest every three hours) did not decrease the incidence of the complaint. Seventy-five percent oxygen produced symptoms in

only 55-percent of the subjects; 50-percent oxygen produced no symptoms during the twenty-four hour period. Since oxygen tents or catheters rarely produce alveolar oxygen concentration higher than 50 percent, these forms of administering oxygen are completely safe. Breathing of 100-percent oxygen at high altitudes (low total atmospheric pressures) does not produce symptoms, indicating that the symptoms are due to high-oxygen tensions and not to elimination of nitrogen. The use of 100-percent oxygen for short periods is probably safe in all patients, but when oxygen must be given in excess of twelve hours the following rules should be followed. The oxygen concentration should be reduced to 60-percent unless this is insufficient to saturate the arterial blood, and when 100 percent oxygen must be administered, a careful check should be made for the symptoms most likely to occur as a result of the high tensions of oxygen.

Comroe, J.H., E.R. Bahnson, and E.O. Coates. Mental changes occurring in chronically anoxemic patients during oxygen therapy. J.A.M.A. 143:1044-1048 (1950).

Cook, S.F., and N.Page. White Mountain high-altitude research station. Science 116:697-700 (1952).

Cook, S.F., and M.H. Alafi. Role of the spleen in acclimatization to hypoxia. Amer. J. Physiol. 186(2):369-372 (Aug. 1956). In order to determine quantitatively the participation of the spleen and the bone marrow in the hypoxic increase in red cell count, five groups of splenectomized and nonsplenectomized mice were exposed to a simulated altitude of 15,000 feet for periods of 30 to 58 days. Red blood cell counts and hematocrit determinations were made at intervals during the exposure. It was found that about two-fifths of the increase in red cells could be referred to a tonic concentration of the spleen and the remaining three-fifths to the production of red cells by the bone marrow.

Cordier, D., and J.F. Worbe. Study on the intestinal absorption of hexoses and pentoses in the frog: II. Influence of oxygen tension on the speed of absorption. C.R. Soc. Biol. (Paris) 149(1-2):110-112 (Jan. 1955). The rate of intestinal absorption of glucose, galactose, fructose, and xylose during hypoxia was determined by measuring the amounts of the administered sugars remaining in the intestines of frogs after exposure for eight hours to an atmosphere of 3 to 3.9-percent of oxygen. Hypoxia was found to decrease significantly the absorption of glucose and galactose, while the rate of absorption of fructose and xylose was unaffected.

Cordier, D., and G. Peris. Proteinemia disturbances induced by altitude and solor radiation. C.R. Soc. Biol. (Paris) 150(1):187-190 (1956). Rats maintained at an altitude of 1800 meters for 17 days showed a marked decrease in the albumin fraction of serum and an increase in the globulin fraction with no change in total protein. After 32 days at altitude, normal serum-protein levels were observed. Repeated one-hour exposures to sunlight had no additional effect on the serum protein of 17-day altitude rats. Two- and one-hour exposures of 32-day altitude rats to sunlight produced a decrease in albumin and an increase in globulin to levels found in rats exposed to altitude for 17 days.

Cordier, P. and G. Peres. Modifications of vegetative nervous equilibrium and of glycemia due to effect of mountain climate. Rev. Med. Swiss. (Rome) 74:220-225 (25 Apr. 1954).

Cori, G.T. Carbohydrate changes during anaerobiosis of mammalian muscle. J. Biol. Chem. 96:259-269 (1932).

Cormack, R.S., D.T.C. Cunningham, and J.B.L. Gee. The effect of carbon dioxide on the respiratory response to want of oxygen in man. Quart. J. Exp. Physiol. (London) 42(3):303-319 (July 1957).

Ventilation, respiratory frequency, and alveolar gas pressures were measured during anoxia in seven men, alveolar carbon dioxide pressure being maintained at or above the normal level. A given degree of anoxia caused a significantly greater respiratory response at a higher level of carbon dioxide pressure in all subjects. This contradicts Gray's hypothesis that respiratory stimuli do not interact.

Cormack, R.S., and J.B.L. Gee. Some respiratory studies on the effect of want of oxygen in man. J. Physiol. (London) 129(3):29P-30P (28 Sept. 1955). A determination of the respiratory response to anoxia alone; without complication by acapnia, was made by continuously adding CO_2 to an anoxic respiratory gas mixture in an amount necessary to compensate for alveolar pCO_2 deficiency. Data obtained from a comparison of ventilation rates with alveolar pCO_2 were found to be inconsistent with Gray's oxygen ventilation equation but consistent with Fitzerald's data on individuals acclimatized to high altitude. When the alveolar pCO_2 was kept constant at 5 or 10 mm Hg. above resting values, the ventilation resulting from anoxia alone was increased. An interaction between CO_2 and anoxic stimuli was thus indicated.

Correa, J., R. Aliaza, and F. Moncloa. Study of adrenal functions at high altitudes with the intravenous ACTH test. School of Aviation Med. AD 126 286, Randolph AFB, Texas. The suprarenal function was stimulated by means of intravenous administration of ACTH in two groups of subjects, healthy native residents in Morococha, at an altitude of 4540 meters (14,900 feet). The response to this stimulation was determined by measuring the urinary excretion of 17-ketosteroids and 17-hydroxycorticoids and the fall in the circulating eosinophils. Well-defined differences were not found between the two groups.

Cosby, R.S. Continuous measurement of alveolo-arterial gradients at ambient and anoxic levels. J. Appl. Physiol. 17(1): 1-5 (1962). In 18 normal subjects, continuous alveolo-arterial differences were measured at decreasing levels in inspired pO_2 from ambient to 12-percent oxygen. A mean difference of 12.1-mm. Hg decreased gradually to virtual obliteration of the gradient at low levels of inspired pO_2. A modified Clark electrode with a Riley needle continuously recorded arterial O_2 tensions and together with a recording alveolar O_2 electrode inscribed a continuous visual alveolo-arterial difference. The response of arterial pO_2 to an anoxic level, though maximal in the first minute (74 percent of the total change in 4 minutes), continued to change at the rate of 2-1/2 percent per minute during and after the fourth minute. Continuously changing levels of ventilation and arterial pO_2 and pCO_2, as described, make it unlikely that the steady state is ever truly present during acute exposure to anoxia.

Cosio, G., and J. Corigleano. Right-ventricular hypertrophy in miners at altitude: I. Non-silicotic miners. Rev. Peruana Card. (Lima) 5 (1):25-38 (Jan.-Apr. 1956). A study was made of 142 electrocardiograms of non-silicotic miners working at 3800 and 4900 meters above sea level. A right-axis deviation was found in 19.7 percent, and a left-axis deviation in 2.1 percent of the miners. In the group showing right-axis deviations, the value varied between 90 and 119 degrees. Signs of right-ventricular hypertrophy were found in 34.5 percent of the cardiograms, and signs of incomplete right bundle-branch block in 14 percent. Some relationship was noted between QRS complex configuration in the V_1 lead and the pattern of the complex in the right $V3_R$ and $V4_R$ leads. The T-wave in the V_1 lead was inverted in 14 percent of the subjects, while 6.3 percent were diphasic 4.2 percent of the electrocardiagrams were isoelectric. The R-wave in the U5 lead was above the maximum limit in 10 percent of the miners, indicating possible left- as well as right-ventricular hypertrophy.

Cotes, J.E. Ventilatory capacity at altitude and its relation to mask design. Proc. Roy. Soc. (London) 143(910):32-39 (Dec. 1954). Experimental data obtained by breathing controlled gas mixtures at simulated altitudes in a decompression chamber, show that the ventilatory capacity of normal subjects increases on ascent to altitude. The major factor influencing the ventilatory capacity is the reduction in air density. The increase is related to the decrease in lung-gas density and is compatible with the hypothesis that the work of maximum breathing remains constant at altitude. An oxygen mask designed for climbers using their full ventilatory capacity is described and its flow resistance compared with that of a low resistance apparatus for measuring a subject's maximum voluntary ventilation.

Cournard, A. The mysterious influence of unilateral pulmonary hypoxia upon the circulation in man. Acta Cardiol. (Brux.) 10(5):429-441 (1955). Using a method combining bronchospirometry, cardiac catheterization, and arterial cannulation, simultaneous determinations were made of total pulmonary blood flow, separate blood flow through each lung, and pulmonary arterial pressures in six subjects breathing an oxygen-poor mixture. Under conditions of moderately unilateral hypoxia no evidence was found of an increased vascular resistance in the ipsilateral lung. Arterial oxygen saturation decreased slightly during the hypoxic periods. Total blood flow was approximately 33 percent above basal metabolic levels, and blood pressure in the pulmonary artery remained unaltered. While subjects breathed with one lung mixtures of 8 and 6 percent oxygen in nitrogen, a notable increase

was observed in total pulmonary blood flow. This change was associated with a drop of arterial oxygen saturation down to 85 percent. No rise was seen in pulmonary artery pressure. Using the same procedures, bilateral hypoxia was induced by administering to both lungs, through separate airways of the bronchospirometer, the same low-oxygen mixture. A drop was observed in arterial blood oxygen saturation down to 64 percent. Mean pulmonary artery pressure rose significantly by 5 mm. Hg.

Creese, R., N.W. Scholes, and W.J. Whalen. Resting potentials of diaphragm muscle after prolonged anoxia. J. Physiol. 140:301-317 (1958).

Cremer, H.D. Physical efficiency in high mountain climate. Klin. Wschr. 22:541 (21 Aug. 1943).

Criscuolo, D., R.T. Clark, and R.B. Mefferd. Cellular adaptation during chronic exposure to hypoxia. AF School of Aviation Med., Report No. 5, (Feb. 1954). Randolph AFB, Texas.

Criscuolo, D., and R.T. Clark. The myoglobin content of various rat tissues as affected by altitude and exercise. AF School of Aviation Med., Report 55-84, Randolph AFB. (Dec. 1955). Rats

chronically exposed to a 20,000 foot simulated altitude showed an increase in myoglobin content of the heart, diaphragm, and gastrocnemius muscles. Exercise did not materially affect this increase. The increase was noted early in the period of acclimatization, about the fourth and fifth weeks; then the values returned to normal at the end of the tenth week. At the tenth week, rats reared at altitude showed about the same myoglobin content as the chronically exposed rats.

Criscuolo, D., H. B. Hale, and R. B. Mefferd. Indices of oxygen transport, utilization, and storage in rats acclimated to altitude at different temperatures. School of Aviation Medicine, Research Project 58-94:1-4, Randolph AFB, Texas (July 1958). Oxygen transport, utilization and storage, and related functions were studied in rats exposed to simulated altitude (18,000 feet) at three different temperatures (5, 24, and 36 degrees Centigrade) for periods in excess of three months. Liver, heart, kidney, and adrenal weights were altered only where thermal influences were involved. Adrenal weight in altitude-cold was greater than in cold alone. The oxygen transport function was normal in altitude-cold, but was depressed in altitude-heat. Liver succinic dehydrogenase activity was elevated in all altitude groups, but more so in both the heat and cold.

The succinic dehydrogenase activity of the adrenals was elevated most in the altitude-cold. Oxygen storage was unaffected by thermal factors.

Criscuolo, D., R. T. Clark, and R. B. Mefferd. Effects of low-and high-iron supplementation on hypoxic rats. Amer. J. Physiol. 80(1):215-218 (Jan. 1955). Rats fed a low- or high-iron dietary supplement survived exposure to a simulated altitude of 20,000 feet for a period of six weeks equally well. A hemoglobin increase seen in the high-iron animals was thus apparently not indispensable for survival. Hematocrits and red cell counts were increased in the low-iron group, indicating that the hemopoietic response in these animals was unaffected. The myoglobin content of various tissue, and oxygen utilization, as reflected by succinic dehydrogenase activity, increased in both groups.

Crisler, G., E. J. Van Liere, and W. T. Booker. The effect of anoxemia on the digestive movements of the stomach. Amer. J. Physiol. 3:629-634 (Dec. 1932). Anoxemia of grades of 10 percent or less, in barbituized dogs, caused inhibition of gastric digestive motility as indicated constantly by a decreased ampiitude of contraction and frequently by a fall in tone. The most plausible mechanism for the early inhibition seems to be a sensitization of the sympathetics by the rise in blood pH that accompanies the initial hyperpnea and hyperventilation in anoxemia. These results are a partial reproduction of the clinical picture of gastrointestinal upsets during venous stasis as seen in cardiac disease. A possible explanation of the discrepancies in the two conditions is mentioned.

Cross, B.A., and I.A. Sivlu. Unit activity in the hypothalamus and the sympathetic response to hypoxia and hypercapnia. Exp. Neurol. 7:375-93 (May 1963). The activity of 232 neurons in the hypothalamus and forebrain regions was recorded with stereotoxically accented steel microelectrodes in rabbits under light urethane anesthesia. Inhalation of N_2 or N_2O for 10 to 30 seconds reduced brain oxygen tension by 30 to 90 percent and accelerated the firing rate of 27 percent of neurons tested. Slowing to hypoxia occurred in 36 percent. Inhalation of 80-percent CO_2 and 20-percent O_2 for 5 to 15 seconds, elevated brain oxygen tension and 90 percent of the neurons tested gave a response to this stimulus. In the hypothalamus, thirty-one of forty-six neurons were accelerated by hypercapnia. A high proportion of tested neurons in the posterior and lateral areas of the hypothalamus were excited by hypoxia, hypercapnia, and pain or auditory stimuli. In addition to the effects on neuron firing, hypoxia and hypercapnia produced a rise in actual pressure, bradycardia and an activation of the electrocardiograms. Similar changes were elicited by electrical stimulation of the sympathetic zone of the hypothalamus. It is suggested that the cerebrovascular supply may be regulated in part by "sympathetic" neurons in the hypothalamus responsive to hypoxia or hypercapnia.

Cross, C.E., P.A. Rieben, C.I. Barron, and P.F. Salisbury. Effects of arterial hypoxia on the heart and the circulation. Amer. J. Physiol. 35:963-970 (Nov. 1963). An integrative series of investigations progressed from simplified systems, where cause-and-effect relations were relatively clear, to the virtually intact animal with separately perfused carotid arteries. Arterial oxygen tension (pO_2) below 40 mm. Hg (about 75-percent oxygen saturation) caused edema of the heart muscle; however the contractile strength and performance of isolated hearts were compromised severely only when the arterial pO_2 had fallen below 15 mm. Hg (about 25 percent saturation). The "acute circulatory crisis" which is known to occur when the arterial oxygen saturation falls below 80 percent was not caused by weakness of the heart muscle but by reflexes from the carotid artery territory. Even when oxygen saturation of systemic arterial blood had fallen as low as

50 percent, heart failure did not result as long as the carotids were perfused with blood of normal pO_2. Severe heat failure occurred when the blood in the carotid arteries was moderately hypoxid (pO_2 below 50, saturation below 80 percent) while the rest of the circulation was fully oxygenated.

Cronson, W. N. and H. T. Linger. A report of physiological changes occurring in respiratory alkalosis at sea level and altitude. Contact 6:17 (1948).

Csalay, L., I. Fenyes, B. Kelentei, and Gy. Ludany. Investigation of pathomechanism of the hypoxic increase in cerebrospinal pressure. Acta Med. Acad. Sci. Hung. (Budapest) 10(4):397-404 (1957). The mechanism responsible for the increase in cerebrospinal fluid pressure in hypoxia was investigated in respect to its susceptibility to various pharmacologic agents. The experiments were conducted with cats under chloralose anesthesia, breathing a six percent O_2 - N_2 mixture. Endogenous histamine mobilization through compound "48/80" increases the cerebrospinal fluid pressure; anti-histaminics (Neoantergan, Antistin, Sandostem, and Synopen) lower the hypoxic response by approximately 30 percent; Ergam and Gynergen which block the sympathetic nervous system and calcium

and Rutin which interfere with permeability are without any effect on the response.

Cuba, A., M. Copaira, E. de la Vega, and B. Pareja. Vitamin E in lambs at altitude. I. Tocopherolemia and blood picture in normal lambs. Rev. Fac. Med. Veterienaria, (Peru) 7-11: 178-184 (1952-1956). Twelve consecutive determinations were made of the blood picture and serum tocopherol in nine lambs at 4000 meters above sea level. The first determination was made between 24 and 48 hours after birth, and the others at intervals of 7, 15, and 30 days. At 60 days, it was observed that the highest values in the number of erythrocytes, hemoglobin, and packed eythrocytes volume coincided with the lowest levels of tocopherol. After 60 days, the hemotological variations tended toward the normal, reaching normal levels in 240 days. It is suggested that these findings constitute a physiological curve in lambs at altitude which is related to a hypotocopherolemic state.

Cuba, A., M. Copain, E. de la Vega, and B. Pareja. Vitamin E in lambs at altitude: II. Tocopherolemia and blood picture in lambs subjected to a vitamin-E deficient diet. Rev. Loc. Med. Veterinaria (Peru) 7-11:185-192 (1952-1956). A group of lambs at 4000 meters above sea level were subjected to a vitamin E deficient diet 48 hours after birth for a period of 5 months, during which time the blood picture and blood tocopherol levels were periodically determined. After 90 days, a marked increase in the number of erythrocytes, hemoglobin, and packed erythrocyte volume was found which persisted until the end of the experiment at 150 days. Aside from polycythemia, the clinical manifestations of mountain sickness or vitamin E deficiency were not observed.

Cullumbine, H., V. Bosnazake, and S. R. Kottegoda. Description of effects produced by residence at moderate altitude. Ceylon Med. J. 8:63-81 (June 1951). Observations made on Ceylonese adults living at moderate altitudes (up to 6200 feet) indicate that such residence is accompanied by an absolute and a relative lymphocytosis, a leukocytosis, and decreased plasma-, blood-, and tissue-fluid volumes. On travelling from sea level to an altitude of 6200 feet, the experimental evidence indicates that there is first an increase in the activity of the adrenal cortex, with a lessened response to adrenalin, and then a decreased activity with enhanced responses to adrenalin.

Cunningham, D. J. C., D. G. Shaw, S. Lahiri, and B. B. Lloyd. The effect of maintained ammonium chloride acidosis on the relation between pulmonary ventilation and alveolar oxygen and carbon dioxide in man. Quart. J. Exp. Physiol. 46:323-334 (1961). Five men ingested about 12g. NH_4Cl daily for about a week. Acidemia was assessed by measuring plasma (HCO_3-) and alveolar pCO_2. Before, during, and after the period of ingestion, the subjects were given various gas mixtures to breathe, and pulmonary ventilation (V) and the alveolar gas pressure (pCO_2,pO_2) were measured in the steady state. The effect of acidemia on the parameters of the equation $V = D\left(1 + \frac{A}{pO_2} - C\right)(pCO_2 - B)$ was examined. Only B which is related to the "CO_2 threshold" was consistently changed, being reduced in acidemia.

Curry, E. T. and F. Boys. Effects of oxygen on hearing acuity at simulated altitude. Eye, Ear, Nose, Throat Monthly 35(4):239-245 (April 1956). Normal subjects breathing supplemental oxygen were decompressed at the rate of 1000-feet per minute and a simulated altitude of 15, 000 feet was reached. Immediately upon arrival at 15, 000 feet and following 30 minutes, hearing thresholds for all frequencies were measured. No statistically significant effect on the audiometric threshold was found at simulated altitude.

Czech, W. Circulatory reactions in cable car trips in the Alps. Med. Klen. (Berlin)49(50):2001-2002 (10 Dec. 1954). This is a comment on a paper published under the above title by E. Hausund and H. Jungmann. The author takes the view that results of experiments using artificial climate chambers (not decompression or pressure chambers) are analogous to those obtained under natural environmental conditions. However, both environments are not to be considered identical in their effects on the human organism. In both cases, the reaction is to the total complex of environmental factors. The author states that he has observed vasomotor and circulatory reactions at altitude differences of 50 meters in the artificial climate chamber. The conflicting results reported by various researchers concerning the appearance of vagotonia during altitude ascent may be explained by the relatively rapid succession of phases and also by the fact that the "initial state of reactivity" of the individual determines the degree of systematic reaction to sudden environmental changes. This reactivity-state is not always evident because of the unreliability of testing methods used, and also because of the possible lack of synchronism between the circulatory responses and changes in the sympathetic tone.

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Daland, J. Altitude sickness result of hemoglobin deficiency. International Clinic 4:124-128 (1923).

Daly, W. J., D. Cline, and S. Bondurant. Effects of breathing oxygen on atrioventricular conduction. Amer. Heart J: 66(3):321-324 (Sept. 1963). Electrocardiographic recordings from 11 normal subjects breathing 100-percent oxygen from a high-flow low resistance mask system for 10 minutes showed small but statistically significant decreases in heart rate. Mean heart rate decreased from 72 ±8 to 66 ±8 ($p = 0.001$). The P-R interval was not affected.

Damasio, R., L. Tabusse, and R. Jolly. Modifications of the electroencephalogram in hypocapnic hypoxemia. Rev. Neurol. (Paris) 82(2):221-224 (1952). Seventy subjects (20 to 46 years of age) inhaled mixtures of 7.5 percent oxygen in nitrogen, corresponding to the oxygen tension at an altitude of 7500 meters. The degree of anoxia was recorded with a Millikan oximeter; at the same time, a six-lead electroencephalogram was registered. The subjects selected for the test fell into three groups: forty subjects were normal; fifteen had neuroses, and fifteen had sequelae of cranialtrauma. With regard to the chronology of oxygen desaturation and the morphology of the encephalographic tracing, the subjects could be grouped according to anoxia sensitivity. Group 0 showed no changes in the EEG until the oxygen content of the blood reached 55 percent. In Groups I, II, III, and IV, delta waves appeared at oxygen saturation of 60, 70, 80 and above 80 percent, respectively. Normal subjects show the best resistance to anoxia between 25 and 35 years. Neurovegetative maturity is not yet reached before the twenty-fifth year and resistance decreases after the fortieth year. Subjects below the age of 25 and above the age of 40 generally belong to Groups II, III, and IV.

D'Amico, G., G. Benda, and M. Chinio. Carbonic anhydrase activity in experimental anoxia. G. Clin. Med. 40(7) 1134-1142. Changes in renal plasma flow, glomerular filtration rate, urinary flow, and tubular Na and K reabsorption after acetazolamide (1 gm. intravenously) have been examined in eight healthy subjects in normal conditions and during experimental hypoxia, induced by inhalation of 10 percent oxygen in nitrogen. Acetazolamide produced its effects (carbonic anhydrase block) also in experimental hypoxia. The results indicate that during insufficient blood oxygen saturation, carbonic anhydrase activity remains at normal levels.

D'Angelo, S. A., Respiratory metabolism of human subjects during prolonged exposures to simulated altitudes of 8,000 and 10,000 feet. Amer. J. Physiol. 146:710-722 (Aug. 1946). Prolonged exposures (10 hours) to simulated altitudes of 8,000 and 10,000 feet without supplementary oxygen and under standardized conditions of restricted food intake increased the respiration of the resting human subject. The degree of respiratory change from the ground level condition was of the same order of magnitude at both altitudes. The augmented respiration involved an increase in depth rather than rate of breathing. The modifications in the respiratory metabolism at altitude were collectively indicative of a respiratory alkalosis. The major changes involved the following: an increase in the minute volume of CO_2 elimination which, relative to ground level values at similar time intervals, became progressively greater with continuing exposure time; an elevation of the respiratory quotient; and shifting of the urinary pH toward alkalinity in individuals displaying appreciable hyperventilation (blowing off of CO_2). No significant

changes in the over-all oxygen consumption or in oral temperature resulted from the protracted exposures at the 8,000- and 10,000-foot levels.

D'Angelo, S.A. Urinary output and phosphorus excretion in human subjects during prolonged exposures at low simulated altitudes (8,000 to 10,000 feet). Proc. Soc. Exp. Biol. Med. 62:13-17 (May 1946).

D'Angelo, S.A. Blood sugar levels and carbohydrate administration in human subjects during prolonged exposures to moderately low altitudes. Amer. J. Physiol. 195:365-375 (Jan. 1946). No significant change from the ground level condition occurs in the blood sugar level of resting human subjects maintained at simulated altitudes of 8,000 and 10,000 feet without supplementary oxygen for periods of 10 hours. The ingestion of pure carbohydrate (dextrose) at these altitudes can cause the development of hypoglycemic reactions secondary to those induced at ground level. These reactions are sufficiently marked so as to affect adversely well-being and efficiency in flight. Carbohydrate tolerance, as measured by the amount of time required for the blood sugar level to attain pre-ingestion values, is not

appreciably altered in human subjects at moderately low altitude. There is suggestive evidence, however, that the homostatic mechanism controlling blood sugar level is affected.

Danhof, I. E., and F. R. Steggerda. Gastric acid secretory response to distention at simulated altitude. Aerospace Med. 32(6):520-523 (1961). The present experiments in human and animal subjects show that hyperventilation induced by simulated ascents to 15,000-foot altitude is accompanied by a lowering of blood carbon dioxide tension and a depression in gastric acid secretion, presumably as a result of intracellular interference with the role of carbon dioxide. Gaseous distention of the stomach under similar conditions of low blood carbon dioxide tension results in an augmentation of gastric acid secretory activity. The mechanism responsible for this augmentation of secretion in response to distention is not identified. The result indicates that the distention stimulus is far more effective in changing the acid secretion in the stomach than in changing the CO_2 content of the blood.

Danishevskii, G. M. Problem of acclimatization of man: general results and prospects of study in the USSR. Vest. Akad. Med. Nauk. SSSR. 13(5):28-37 (1958).

Danopoulos, E. D. The pathophysiological phenomena of high altitudes. Hellen. Iatr. 32:3-21 (Jan. 1963).

d'Arcangelo. Cardiopathies of Eritrean natives: pathogenetic, clinical and statistical study. Boll. Soc. Ital. Med. 5(5-6):231-246 (1945).

Das, S.K. Mountaineering and nutrition. Armed Forces Med. J. (Pooma) 18(4):526-534 (Oct. 1962). The nutritional aspects of the Indian Mount Everest Expedition (1960) are discussed, taking into consideration the problems of hypoxia, dehydration, and psychology which are prevalent at high altitude. Performance at high altitude was better on a high-carbohydrate diet. Carbohydrates, being oxygen-rich, decreased the oxygen requirement for work. Protein intake did not appear to influence performance capacity, and in a well-balanced diet the protein requirement was easily met. No difference was found between the vegetarians and the non-vegetarians. Vitamin dietary supplements were beneficial. Coffee, tea, or other beverages containing caffeine had a stimulating effect, but their use in large amounts was not recommended. The use of salt in excess of that contained in the meal was necessary only under unusually hot conditions. Extra water was necessary at high altitudes. Nutrition in mountaineering is related to the type of activity performed at different stages (approach march, acclimatization camp, base camp, higher camps, and return journey), to the nutritional status of the subject at the outset, and to the effect supplementation may have on performance. The diets used by the British Cho Oyo Expedition (1952), British Mount Everest Expedition (1953), and the Indian Mount Everest Expedition (1960) are analyzed.

Das Gupta, C. R. Blood picture of the Indian at high altitudes. Indian Med. Gaz. 87:95-100 (March 1952). The blood picture of Indians living at high altitude was studied at Kalempong (3,933 feet), Sheilong (4978 feet), Upper Sheilong (5900 feet), and Gagtok, Sekkim (5900 feet).

Davis, P.A., H. Davis and J. Thompson. Progressive changes in human electroencephalogram under low-oxygen tension. Amer. J. Physiol. 123:51-52 (1938).

Davis, B.O. Indirect measurement of mean venous oxygen tension during anoxia. J. Clin. Invest. 23:666-675 (Sept. 1944).

Dedyulin, J.M. Coupled ion exchange of potassium and sodium salts between human erythrocytes and blood plasma at various partial oxygen pressures. AFSC N65-17816, Foreign Technology Div., Wright-Patterson AFB; Ohio. The potassium concentration of blood plasma in man is higher at high altitudes than at near sea level. The reduction of carbonic acid in the pulmonary circulation and the ensuing alkalosis leads to an increase in potassium concentration in the peripheral blood. This fact indicates an absorption mechanism of the cell membrane permeability and suggests hemoglobin and oxyhemoglobin as the basic buffer system of the sodium-potassium shift between the erythrocytes and plasma.

Defaut, A. Climatic factors in high mountain resorts. Wien. Med. Wschr. 106:204-206 (3 Mar. 1956).

Dejmal, V. New discoveries and problems in the realm of high-mountain physiology. Teorie a Praxe Telesne Vychovy a Sportu (Prague) 5(10):596-603 (1957). A discussion is presented on the effect of elevated altitudes on the human organism. In comparison with air force physiology, high mountain physiology and physiological observations carried out during a mountain expedition are rather poor since the primary objective is sports achievement. It is only in recent times that the physician and the physiologist have become an

integral part of an expedition. Acclimatization and individual altitude tolerance have a greater importance for mountaineering than the age factor; the best years are considered to be in the early thirties. A simple and reliable criterion is needed to differentiate between the failure of the neurocirculatory mechanism, metabolic failure, and the exhaustion of caloric reserve. A medical treatment after early discovery of a pathological state constitutes a further problem.

Dejours, P., R.H. Kellogg, and N. Page. Regulation of respiration and heart rate response in exercise during altitude acclimatization. J. Ap Physiol. 18:10-18 (Jan. 1963). In three subjects, pulmonary ventilation, alveolar gas, blood lactate, and heat rate were studied at rest and during two grades of treadmill exercise in four (sic) environmental conditions: at sea level breathing air of 13 percent oxygen (simulating altitude), and during a sojourn of three weeks at an altitude of 3,800 meters breathing air with 33 percent oxygen (simulating sea level). At altitude, ventilatory response to exercise was decreased by inhalation of 33 percent oxygen but remained above that observed while breathing air at sea level. Study of the transients at the beginning and end of exercise showed that in all four environmental conditions, the ventilatory response to exercise could be dissected into fast and slow components, interpreted as neurogenic and humoral, respectively, in accordance with the neurohumoral theory. In two subjects, an increased hyperpnea of exercise at altitude represented increases in both the neurogenic and humoral components, while in the third subject, only the humoral components were increased. Study of the composition of alveolar gas at the start and end of exercise indicated that pulmonary blood flow, as well as ventilation, undergoes immediate change at these times. Resting blood lactate concentrations and the increment produced by exercise were higher at altitude. Resting heart rate tended to increase throughout the altitude sojourn in these subjects. The increment in pulse rate produced by exercise fell progressively, as expected.

Dejours, P., F. Girard, Y. Labrousse, R. Molimard, and A. Teillac. Existence in man of an oxygen stimulus of ventilation after acclimatization to an altitude of 3613 meters. C. R. Acad. Sci. (Paris) 245(26):2534-2536 (Dec. 1957). A simple oxygen test (inhalation of pure oxygen) was administered to three subjects acclimatized to an altitude of 3613 meters for 6 to 19 days. Oxygen breathing acted as a stimulus reducing pulmonary ventilation by 39 percent for a short period. This stimulus controlled half the ventilatory output and showed no tendency to decrease in intensity during acclimatization and did not eliminate the carbon dioxide-pH stimulus which also controlled part of the ventilatory output at altitude after acclimatization.

Dejours, P. Recent advances concerning alveolar respiratory exchanges. J. Physiol. (Paris) 46(2):679-700 (1954). Equations for alveolar air and alveolar ventilation are reviewed along with the concept of blood-flow relationships and mean alveolar air and ventilation during respiration. Alveolar air during voluntary apnea, voluntary hyper-ventilation, hypoventilation, and anesthesia is discussed and respiratory adaptation to altitude is evaluated.

Dejours, P., F. Girard, Y. Labrousse, and A. Teillac. Regulation of resting ventilation in the human at high altitude. Etud. Franc. Rev. Clin. Biol. 4(2):115-127 (Feb. 1959).

Delangen, C. C. Hypoxemia and myoglobin. Aeromed. Acta (Soesterberg) 5(1956-57):355-358 (1958). The myoglobin content of the muscles of the hind leg of rabbits was studied before and after subjec-to a 7000-meter simulated altitude for 4 days. An increase

of myoglobin was observed, which was found to be proportionately higher than the increase of hemoglobin in the blood. It is suggested that this represents an important mechanism of adaptation to conditions of anoxemia.

Delius, L., E. Opitz, and W. Schoedel. Adaptation on Monte Rosa; Studies during muscular exertion. Luftfahrtmedizin 6:225 (1942).

Delrue, G. Effect of high altitude on gastric acidity. Arch. Int. Physiol. 38:126-137 (April 1934).

Delrue, G. Changes in acid secretion of stomach during sojourn in high altitude. C. R. Soc. Biol. 113:940-942 (1933).

Delrue, G., and A. Vescher. Changes in amount of glutathione in blood during sojourn in high altitude. C. R. Soc. Biol. 113:942-944 (1933).

Dell, D. B. Effects of physical strain and high altitudes on heart and circulation, Lewis A. Conner Lecture. Amer. Heart J. 23:441-454 (April 1942).

Denver, Michael. Oxygen Lack. Flying 53(4):33, 60 (Oct. 1953). "Queer things happen when you don't get enough oxygen. It's like being a little tight, in the early stages. You become exhilarated, giggly, and over-confident; at the same time, your judgement becomes unreliable. You become somewhat irresponsible and you may even have hallucinations." The author describes a personal incident in which he did not realize he was flying with insufficient oxygen.

Deschwander, J. von. Pain perception in high altitude. Acta Neuroveg. (Wien) 7:371-373 (1953).

Dexter, L. Congenital defects of the heart in high altitudes. New Eng. J. Med. 247(22):851-852 (27 Nov. 1952). A high incidence of patent ductus arteriosus observed in Mexico City (altitude 7,500 feet) and in the district of Junin, Peru (10,000 feet) suggests a correlation between these congenital anomalies and high altitude. It has been observed in these localities that communicable diseases such as rheumatic fever and subacute bacterial endocarditis are rare (but not typhus); eruptive diseases such as German measles are practically nonexistent.

Di Giorgio, A. M. The struggle to conquer high altitude. Minerva Med. (Torino) 46(2):686-689 (March 1955). No significant changes in respiratory activity were observed in mountain climbers and various subjects at sea level (Torino), or at high altitudes (Plateau Rosa, 3500 meters). However, an increase in respiratory activity was noted when the subjects rebreathed a mixture of 7.5-percent oxygen in nitrogen at sea level or rebreathed environmental air at high altitude. Both at sea level and at high altitudes cardiac frequency was found to be normal in most subjects and somewhat lower in others. During rebreathing of oxygen-deficient mixtures, cardiac frequency showed an increase and electrocardiographic tracings indicated a reduction of electrical diastole and modifications in the T wave. No significant changes in oxygen consumption were demonstrated in hypoxic conditions.

Dill, D.B., H.T. Edwards, and A. Folling. Adaptations of the organism to changes in oxygen pressure. J. Physiol. (London) 71:47-63 (1931).

Dill, D.B. Hypoxia: high altitudes revisited. Med. Thorac.

Dill, D.B., S. Robinson, B. Balke, and J. Newton. Work tolerance: age and altitude. J. Appl. Physiol. 19(3):483-488 (May 1964).

Dill, D. B., J. H. Talbott, and W. V. Consolazio. Man at high altitudes. J. Biol. Chem. 118:649-666 (1937).

Dill, D. B., J. W. Terman, and F. G. Hall. Hemoglobin at high altitude as related to age. Clin. Chem. 9:710-716 (Dec. 1963). During the summer of 1962, the early phase of acclimatization to high altitude was studied in six members of the 1935 International High-Altitude Expedition to Chile. Ages of the six ranged from 58 to 71. Two members had also taken part in a high-altitude study in 1929. In their earlier years, these subjects had an increase in hemoglobin concentrations beginning with arrival at high altitude. This response has been well established, especially by the Pike's Peak party led by Haldane and the work of Hurtado and associates in Peru. On the other hand, five of the six members in the 1962 party exhibited a decrease in hemoglobin concentrations during the first few days. The greatest decrease was observed in the oldest subject. His hemoglobin was 88 percent of his sea-level value after 9 days at altitude and remained below his sea-level value for another week. No observations were made on blood volume; hence, one can only speculate regarding possible related changes.

Dill, D. B. Gas equilibria in the lungs at high altitudes. Amer. J. Physiol. 115:530-538 (1936). The opinion of Krogh, Barcroft et al, that diffusion can account for the transfer of oxygen in the lungs, is fully confirmed. At high altitudes, the partial pressures of oxygen in arterial blood, measured by referring its percentage saturation with oxygen to the dissociation curve of the same specimen of blood, is approximately equal to that in alveolar air. The oxygen saturation of arterial blood does not necessarily increase during acclimatization. Men who have lived for years at 5.34 kilometers have a saturation range from 67.6 to 84.6 percent. "Our own values after only a few days at this altitude were within the same range and had the same average value."

Dill, D. B., and J. L. Newton. Respiratory adaptations to high altitudes as related to age. I. Relations of development and aging. Presented at the fifteenth Annual Meeting of the Gerontological Society, Miami Beach, Fla; Berren, James (ed.) pp. 115-127. Springfield, Ill.: Charles C. Thomas, 1964. The adaptation of six men to high altitudes has been compared with their responses to altitude twenty-seven years previously. In this report, special attention has been given to respiratory adaptations in rest and

exercise. The respiratory minute volume in rest increases about as rapidly and to the same extent as in young men. Nevertheless, several of the six subjects were slower to acclimatize than before, as indicated by dyspnea on exertion, headache, Cheyne-Stokes breathing and associated loss of sleep. In exercise, easy work on the ergometer was performed with the same respiratory minute volume as in 1935. As the grade of work was increased, the minute volume increased more than in 1935; the oxygen consumption in peak performance was much less than in 1935.

Dill, D.B., H.T. Edwards, and W.V. Consolazio. Blood as a physico-chemical system: XI. Man at rest. J. Biol. Chem. 118:635 (1937).

Dill, D.B., J.H. Talbott, and W.V. Consolazio. Blood as a physico-chemical system: XII. Man at high altitude. J. Biol. Chem. 118:649 (1937).

Dill, D.B. Reunion at high altitude. Physiologist 6:40-43 (1963).

Dill, D.B. Effects of physical strain and high altitudes on heart and circulation (Lewis A. Conner Lecture). Amer. Heart J. 23:441-454 (Apr. 1942).

Dines, J.H., and E.P. Hiatt. Prolonged exposure of young rats to an oxygen atmosphere at reduced pressure. J. Appl. Physiol. 19(1):17-20 (Jan. 1964). This investigation studied the effect of exposing 12 young male white rats to an atmosphere almost free of nitrogen but with alveolar pO_2 similar to that of the 12 control animals breathing ambient air. This was achieved by keeping the experimental animals in almost pure oxygen at a reduced pressure. Experimental and control animals were in closed chambers with oxygen being supplied from a spirometer while CO_2 was being absorbed. Humidity and temperature were closely regulated. Provision was made for handling the animals and supplying them with food and water without changing the chamber environment. A successful experiment lasting 24 days was completed, not including observation periods of 6 days before and 8 days after the experiment when both groups were kept in air. No consistent difference was noted in rate of growth, oxygen consumption, food consumption, water intake, hemoglobin concentration, or behavior of the two groups. A decreased rate of urine production by the rats in the experimental group was attributed to an increased evaporative loss of water in the rarefied atmosphere.

Dirkin, M. N. J., and H. Humstra. The adaptation of the lung circulation to the ventilation. Quart. J. Exp. Physiol. 34:213 (1948).

Dolina, S. A., and G. P. Konradi. Influence of hypoxia on propagation of stimuli in the respiratory formations of the brain. AFSC N65-17766, Foreign Technology Div., Wright Patterson AFB, Ohio. Rats with electrodes permanently implanted into the motor projection center of the frontal lobe of the cerebral cortex were subjected to hypoxia in a pressure chamber, in which various altitudes were simulated through sudden drops in pressure. Animals that exhibited convulsions upon electrical stimulation of the motor area showed an increased stimulation threshold at lower pressures. Their sensitivity to the effects of the central nervous system stimulants was increased with a slight decrease to ambient pressure. The results showed that moderate hypoxia, which does not lower the oxyhemoglobin concentration of the blood, increases the response threshold at the motor loci and helps to maintain the normal relationship of the activity of the cortical center.

Dombrovskaya, Yu. F., A. S. Chechulin, A. N. Dombrovskiy, and A. A. Rogov. Significance of hypoxemia in the pathology of childhood.

AFSC N65-17762, Foreign Technology Div., Wright-Patterson AFB, Ohio. Hypoxemia and respiratory insufficiency lie at the roots of childhood pathology in a number of illnesses. Through clinical study of young children with pneumonia and experimental studies on rats, it was established that asphyxia sets up a pre-morbid state for the development of pneumonia. Also, under conditions of oxygen starvation, changes typical of chronic interstitial pneumonia were observed. Furthermore, in children attending rural schools, data indicated that disturbances to external respiration and gas composition of the blood were considerably less severe. Therefore, in cases of pathogenetic treatment particular attention should be given to latent or manifest hypercapnia and hypoxia occurring in childhood illnesses. The aerotherapy widely employed in children's clinics bears witness to the expediency and effectiveness of fresh air therapy.

Douglas, C.G., C.R. Greene, and F.G. Kergin. The influence of ammonium chloride in adaptation to low barometric pressures. J. Physiol. (London) 78:404-414 (1933).

Douglas, C.G., J.S. Haldane, Y. Henderson, and E.C. Schneider. Physiological observations made on Pike's Peak, Colorado, with special reference to adaptation to low barometric pressure. Trans. Roy. Soc. 185-318 (1912).

Douglas, C.G. Pulmonary function (historical): Respiratory physiology in aviation. School of Aviation Med., AD 49 179, Randolph AFB, Texas. This is a historical survey of various aspects of the complex pulmonary physiology relevant to aviation medicine, discussing in turn various approaches to the etiology of hyperpnea, effects of high and reduced barometric pressure, effects of CO_2 on respiratory centers and its relationship to hydrogen ion concentration of the blood, muscular work, and lactic acid concentration. The functional regulation of breathing and related aspects are reviewed, including periodic breathing, the identification of chemoreceptors in the aortic and carotid bodies, composition and measurement of alveolar air, and the relationship between hyperpnea and muscular exercise. Acclimatization at high altitude involves the following problems; the dissociation of oxyhemoglobin, the effect of reduced O_2 pressure above 10,000 feet, and the significance of uneven ventilation.

Downey, S. E., J. P. Remenshyder, and J. H. Mitchell. Cardiovascular responses to hypoxic stimulation of the carotid bodies. Circ. Res. 10:676 (1962). The hemo-dynamic responses to hypoxic stimulation of the carotid bodies were investigated in a dog with controlled respiration. A dual rotating disc oxygenator system was utilized to perfuse the vascularly isolated carotid region alternately with blood of high or low pO_2. Perfusion of the carotid bodies with hypoxic blood caused a large reduction of heart rate. The bradycardiac response was reduced, but not abolished, by vagotomy. However, the subsequent administration of hexamethonium completely abolished the response. The contractility of the atrium was reduced by carotid body hypoxia, and varying degrees of heart block were frequently observed.

Downing, S. E., J. H. Mitchell, and A. G. Wallace. Cardiovascular responses to hypoxia and to ischemia of the central nervous system. Abstract in Fed. Proc. 21(2):139 (1962).

Doyle, J. T., J. S. Wilson, and J. V. Warren. The pulmonary vascular responses to short term hypoxia in human subjects. Circulation. 5(2):263-270 (1952). A group of 8 normal subjects breathing an air mixture containing 10-percent oxygen for about 10 minutes, showed

rapid reduction (to about 75 percent) of the arterial oxygen saturation, causing a considerable increase in pulmonary vascular resistance and cardiac output. This increase in resistance is attributed to the effect which the low oxygen tension of the returning venous blood has on the walls of the pulmonary arterioles. The increase in cardiac output is a compensatory reaction. The same experiments were repeated on a group of subjects affected with cardiopulmonary disturbances, and among the deviations from the reactions of the normal subjects were the following; smaller increases in pulmonary vascular resistance and no increase in the cardiac output.

Dreyfus, C. Anoxia and blood. Bull. Fed. Gynec. Obstit. Franc. 4(1 Bis): 270-271 (1952). Studies on the correlation between anoxia and erythropoiesis are briefly reviewed and comparisons are made between the various theories on the underlying physiological mechanism.

Dripps, R.D., and J.H. Comrof. The effect of inhalation of high and low oxygen concentrations on respiration, pulse rate, ballistocardiogram and arterial oxygen saturation (oximeter) of normal individuals. Amer. J. Physiol. 149:277-291 (1947).

Dubs, J. Peculiarities of army medical service in mountains. Med. Welt. 9:1507-1512 (19 Oct. 1935).

Duckworth, M. W. Changes in oxygen consumption and cytochrome c in the diaphragm of acclimatized rats. J. Physiol. (London) 152:55-56 (1960).

Duckworth, M. W. Tissue changes accompanying acclimatization to low atmospheric oxygen in the rat. J. Physiol. (London) 156:603-610 (May 1961).

Duff, A. W. The acclimatization of mountaineers to the high altitudes of the Himalayas. McGill Med. J. 27(2):74-88 (Apr. 1958). The acclimatization of mountaineers to the high altitudes of the Himalayan mountains is a complex physiological process which involves, primarily, the response of the respiratory and circulatory systems to the reduced atmospheric pO_2 but affects all other systems. The circulatory system is responsible for the greatest single adaptation during acclimatization. The inherent dissociation characteristics of oxyhemoglobin causes this adaptation. The respiratory system responds with an increase in pulmonary ventilation which brings more oxygen to the alveoli, causing great reductions in the pO_2

gradient from atmosphere to tissues so that the tissues can function at near-normal oxygen tension in spite of the altitude. During ascent to high altitude, satisfactory acclimatization occurs up to an altitude of 23,000 feet, above which rapid deterioration takes place. The process of adequate acclimatization requires three to four weeks during which the mountaineer gradually ascends to an altitude of approximately 21,000 feet with frequent trips to lower altitude. Oxygen is a tremendous aid at high altitude and is effectively an "altitude reducer."

Dugal, L. P., and P. E. Fiset. Sensibility of man to light anoxia. Aviation Med. 21:362-374, 404 (Oct. 1930). Human subjects submitted repeatedly to a simulated altitude of 10,000 feet (over a period of several weeks), improved their scores in a very significant way in many psychological tests when they received extra oxygen (by demand valve) at altitude. Control subjects receiving compressed air (by the same system) showed no significant progress in the same tests. The same results were found during two consecutive years on two different groups of 20 human subjects for three of the principal psychological tests used; namely, the MacQuarrie test for Mechanical Ability, the Survey of Space Relations Ability, and the

Survey of Object Visualization. Other tests, tried only during the last experiment, gave the same results. Some of the tests showed no progress or equal progress for both groups, but there was no instance where the group submitted to mild anoxia (not receiving added oxygen at 10,000 feet) could display a better performance than the group receiving oxygen. On the contrary, the latter improved in a significant way from test to test in the majority of cases. All results seem to indicate that the relative deficit of oxygen, corresponding to an altitude of 10,000 feet, inhibits partly the normal functioning of the higher centers, especially the learning process.

Duke, H. N., Site of action of anoxia on pulmonary blood vessels of the cat. J. Physiol. (London) 125:373 (1954).

Duke, H. N., and E. M. Kelleck. Effect of anoxia on pulmonary arterial pressure. J. Physiol. (London) 114:3p (1951).

Dumas, A. Effects of high altitude and climate in disturbances of heart and circulation. Presse Therm. Climat. 73:274-276 (15 Apr. 1932).

Dumke, P. R., C. F. Schmidt, and H. P. Chiodi. The part played by carotid body reflexes in the respiratory response of the dog to anoxemia with and without simultaneous hypercapnia. Amer. J. Physiol. 1:1-20 (May 1941).

Dunn, J.M. Psychomotor functioning while breathing varying partial pressures of oxygen-nitrogen. School of Aerospace Med., N62-17360, Aerospace Med. Div., Brooks AFB, Tex. (June 1962). To examine the proposition that gaseous nitrogen produces some degree of narcosis under normal or reduced pressures, 70 subjects were tested on a multidimensional pursuit task while breathing various oxygen-nitrogen mixtures. The partial pressure of nitrogen was reduced in two ways; by increasing the oxygen percentage in the mixture while maintaining constant total pressure, or by decreasing the total pressure while maintaining a constant partial pressure of oxygen. There were no significant changes in performance that could be regarded as correlated with the nitrogen variable. However, increments in the partial pressure of oxygen lessened significantly the rate and magnitude of performance decrement, as noted by previous investigators.

Durig, A. Physiology and pathology of climate at moderate altitude. Wien. Klin. Wschr. 50:11-17 (8 Jan. 1937).

Durnin, J. V. G. A. Oxygen consumption energy expenditure and efficiency of climbing with loads at low altitudes. J. Physiol. (London) 128:294-309 (27 May 1955). The energy expenditure of two subjects while climbing was determined. Climbing was done on two measured gradients on Ben Lomand. Four different loads weighing 5, 10, 15 and 20 kilograms were carried daily on the two gradients for a period of 8 days: The complete experiment was arranged in the form of an 8 times 8 latin square. Results were tabulated for the energy expenditure, oxygen consumption, and pulmonary ventilation. The coefficient of variation was about four percent. The respiratory quotient, efficiency of climbing, and the oxygen extraction were also tabulated. The negative relationship between pulmonary ventilation and oxygen extraction was discussed.

Dyborvski, W. Conditions and limits of acclimatization to altitude in aviation. Polska Cgaz. (Lek.) 13:5-8 (1 Jan. 1934).

E

Eastman, J. N. Mount Everest in utero: President's address. Amer. J. Obstet. Gynec. 64(4):701-711 (Apr. 1954). The history, physiology, and clinical symptoms of high-altitude anoxia are reviewed, beginning with the observations of Marco Polo when he crossed the plateau of Pamir, in Central Asia in 1298, and continuing through the extensive and detailed information provided during the second World War, and evolving through the important data acquired in mountain-climbing expeditions during the 1950's. Both environmental conditions at high altitudes and the processes of acclimatization are compared with the environment and adaptation processes of the fetus in utero. This environment of the fetus in utero corresponds to an atmosphere in which the partial pressure of 0_2 is the same as that which exists 3/4 of a mile above Mt. Everest (i.e., 33,000 feet) or, at an 0_2 pressure of 30 mm. Hg. The fetus compensates, as does an adult, by a pronounced increase in hemoglobin value up to approximately 17 gr./100 cc. (approximately 20 percent higher than that obtained in the average adult or child). This approaches the degree of acclimatization which Haldane and Henderson found developed in

those who resided at 14,000 feet altitude for about a month. Fetal blood also resembles that of mountaineers in showing other evidence of increased bone marrow activity, i.e., the presence of nucleated red cells, polychromatophilia, anisocytosis and poikilocytosis.

Ebert, R. V., C. W. Borden, H. S. Wells, and R. H. Wilson. Studies of the pulmonary circulation. I. The circulation time from the pulmonary artery to the femoral artery and the quantity of blood in the lungs in normal individuals. J. Clin. Invest. 28:1134 (1949).

Eckman, M., B. Barach, C.A. Fox, C.C. Rumsey, and A.L. Barach. Effect of diet on altitude tolerance. Aviation Med. 11:328-340 (Oct. 1945). Studies were made on the effect of diet on altitude tolerance at levels of 15,000 and 17,000 feet. An increase of approximately 1,000 feet in altitude tolerance is indicated by changes in the arterial blood gases after ingestion of a high carbohydrate as compared to a high fat-protein meal. An increase of between 1,300 and 1,400 feet in altitude tolerance is indicated by changes in the alveolar gases after ingestion of a high carbohydrate as compared to a high protein-fat meal. Tests of psychomotor and physiological performance under the conditions detailed above, show that a gain

of between 1,000 and 2,000 feet is achieved following the high carbohydrate meal. Changes in the individual while approaching equilibrium, or a steady state, do not appreciably affect the degree of altitude gain. When subjects are permitted to choose the quantity and type of food they prefer, their altitude tolerance is decreased only to the extent of approximately 500 feet below that following the special high carbohydrate meal. The gain in altitude tolerance with the high carbohydrate diet appears to be due to the increased RQ — a higher production of CO_2 with a given oxygen consumption theoretically resulting in a proportionate rise in alveolar ventilation and pO_2. The determined sum of arterial pO_2 and pCO_2 was 76.4, 73.0, and 75.8 mm. Hg with the high carbohydrate, the high protein-fat meal, and the meal of choice respectively. When one hundred-percent oxygen is breathed, no benefit would be expected from a high carbohydrate diet.

Eckstein, J. W., and A. W. Hersley. Effects of hypoxia on peripheral venous tone in man. J. Lab. Clin. Med. :847-853 (Dec. 1960). Venous pressure-volume curves were obtained from the

forearm with subjects breathing air, 11.5-, and 7.5-percent oxygen in nitrogen. There were insignificant changes in venous tone with 11.5-percent oxygen, but active venous constriction occurred regularly with the 7.5-percent mixture. This constriction was sufficient to displace small amounts of blood from the extremity. The change in venous tone could not be attributed to the required hyperventilation which occurred with low oxygen breathing.

Edwards, H. T. Lactic acid in rest and work at high altitude. Amer. J. Physiol. 116: 367-375 (July 1936).

Efendiev, M. E., S. M. Bedaldva, and D. K. Akhundov. Effect of mountain conditions on arterial pressure. Klin. Med. (Moscow) 37:59-62 (July 59).

Eggers, H. Human blood picture in Mexico. Munchen Med. Wschr. 73:779-781 (7 May 1926).

Ehrlich, R. Effects of air contamination at high altitudes on sensitivity to infection. Rev. Med. Aero. (Paris) 2:103-105 (Feb.-Mar. 1963).

Elliot, R. V. Ballistocardiography at simulated altitudes. J. Aviation Med. 26(2): 137-145 (Apr. 1955). Twenty-six young healthy adult

subjects were evaluated ballistocardiographically at ground level when breathing a mixture of 10-percent oxygen in nitrogen, and at simulated altitudes of 10,000, 20,000, 30,000, and 40,000 feet using standard oxygen equipment at all levels. The subjects remained in a supine position on the steel floor of the low-pressure chamber throughout the entire experiment, and ballistocardiograms were obtained with the portable electromagnetic ballistograph. When simultaneous electrocardiogram tracings were obtained with all ballistocardiograms, changes were not significantly altered in 25 of the 26 subjects during any phase of the experiments except for acute hypoxia.

Ellis, J. P., and J. G. Wells. The detection of in-flight hyperventilation by blood and urine analyses. USAF School of Aerospace Med., Tech. Report No. 62-117, Aerospace Medical Div., Brooks AFB, Texas (Nov. 1962). An alternate method for the detection of in-flight hyperventilation in pilots was investigated. The method, based on the measurement of several acid-base related components in blood and urine, was found to be more convenient and practical than the previously described method based on the measurement of PA_{CO_2} in end-expired air samples collected during flight. The data indicated that when a relatively small degree of hyperventilation is experienced by pilots, as indicated by the in-flight PA_{CO_2}, the corresponding small change in blood and urine components is insignificant. However, when the in-flight CO_2 indicates a greater degree of hyperventilation, blood and urinary variables are significantly changed. Thus, it is concluded that the method can detect hyperventilation at a level of concern.

Ellis, V. C. Plasma and total blood volume estimations by the T1824-hematocrit method: the normal values of the Witwatersrand (altitude 5704 feet). S. Afr. J. Med. Sci. 18(2):45-56 (Sept. 1953). A modification is described for the T1824 method of determining the plasma volume in man, using the Evelyn macro-colorimeter at the 6-ml. aperture. The accuracy of the photoelectric method is increased by a gravimetric technique which involves the weight of dye solution administered. In vitro experiments show the mean error of this technique to be 2.1 percent with an observed maximum deviation of 2.8 percent. The plasma volume for 20 healthy South African European males living on the Witwatersrand at 5,740 feet above sea level was 39.3 ± 0.649 ml/kg, the total blood volume was 75.1 ± 1.21 ml./kg. and the red-cell volume was 35.8 ± 0.816 ml./kg. On comparison with American and English sea-level

workers, the plasma volume of these subjects is reduced by about 13 percent, the total blood volume by about 8 percent, and there is no significant difference in the red cell volumes. It is suggested that the cause of the reduced plasma volume is the lower barometric pressure at this altitude. Furthermore, this plasma volume reduction may increase the oxygen carrying capacity per unit volume of the blood sufficiently to offset the existing relative anoxia at this altitude. Plasma volume reduction produced no observed increase in the volume of circulating red cells.

Ellis, F.P., H. M. Ferres, A. P. Lind, and P. S. Newling. The upper limits of tolerance of environmental stress. Med. Res. Counc. Spec. Rep. (London) 298:158-179 (1960).

Ellis, B. C. A comparison of the T1824 blood volume at sea level and an altitude of 5740 feet in normal South African European males. S. Afr. J. Med. Sci. 19:1-2 (June 1954). The results of single blood volume estimations on 20 healthy South African European males who were living at sea level are presented. The plasma volume was 43.5 ± 0.77 ml./kg., the red cell blood volume 36.6 ± 0.82 ml./kg., and the total blood volume 80.1 ± 1.42 ml./kg. These values fall within the normal range given for sea-level values elsewhere when

the results of the Cape Town (sea-level) and Johannesburg (5740 feet) series are compared, the differences previously suspected by the author are confirmed. Comparison of the ml./kg. values shows that plasma volume is reduced by 9.7 percent at Johannesburg, the total blood volume is lower by 6.2 percent, and the red cell volume is essentially the same as at Capetown. The altitude difference appears to be responsible for these changes. It is suggested that the hemoconcentrations at a moderate altitude correct the associated relative anoxia. As a result, no increase in the red cell mass occurs.

Elsner, R. W., and A. Bolstad. Thermal and metabolic responses to cold of Peruvian Indians native to high altitude. Artic Aeromedical Lab., Report No. AAL-TDR 62-64, Aerospace Medical Div., Fort Wainwright, Alaska (June 1963). Thermal and metabolic responses of eight male Peruvian Indians, native to an altitude of 4000 to 4500 meters, were studied during night-long exposures to moderate outdoor cold (2° to 5° C.). In addition, four of the subjects were studied during cold exposure while chewing coca leaves, which they alleged to have protective effects during cold exposure. The metabolic rate of the eight subjects was elevated during cold exposure but did not differ significantly from averaged values for 17

Caucasian control subjects studied under similar conditions in previous experiments. Differences between the thermal responses of the Indian subjects and of the same Caucasian controls were noted in the generally higher hand and foot temperatures, and the correspondingly lower rectal temperatures of the high altitude dwellers. The Indian subjects using coca did not display any measurable differences in their responses, with or without the drug. However, by observation, and by their own report, they did sleep longer and more comfortably when using coca.

Engel, G. L., J. Romano, J. P. Webb, H. W. Ryder, E. B. Ferris, and M. A. Blankenhoven. A migraine-like syndrome associated with exposure to high altitude. Proc. Centr. Clin. Res., 16:86(1943).

Engel, G. L., E. B. Ferris, C. D. Stevens, M. Logan, and J. P. Webb. The syndrome of hyperventilation. J. Lab. Clin. Med. 31:474-475 (1946).

Ensing, H. Causes and symptoms of high-altitude sickness. Geneesk, Tijdschr. V. Nederl-Indie. 81:651-676 (25 Mar. 1941).

Ernsting, J. The ideal relationship between inspired oxygen concentration and cabin altitude. Aerospace Med. 34(11): (Nov. 1963).

This study reviews the factors which determine the physiologically desirable relationship between the concentration of oxygen in the inspired gas and the absolute pressure within a pressurized or sealed cabin. The minimum acceptable concentration of oxygen at a given cabin altitude is determined by the need to prevent both hypoxia in the steady state and following a sudden decompression. The maximum allowable concentration of oxygen is influenced principally by the direct toxic effects of oxygen upon the respiratory tract, and by the need to reduce the possibility of gross pulmonary atelectasis in the presence of blockage of the airways induced by exposure to accelerative forces. The incidence of decompression sickness is the main factor which limits the maximum cabin altitude. It can also influence the composition of the gas breathed in the intact cabin if depressurization of the cabin or the use of a full pressure suit must be considered. Although conflict between these various requirements exist in certain areas, the physiological ideal at cabin altitude below 20,000 feet is an inspired oxygen concentration of 50 percent.

Ershler, I., C. E. Kossman, and M. S. White. Venous pressure and circulation time during acute progressive anoxia in man. Amer. J. Physiol. 138:593 (1943).

Esipenko, B. E. Influence of high mountain factors on the reflex relationships between renal and salivary activity. AFSC N65-17822, Foreign Technology Div., Wright-Patterson AFB, Ohio. Dogs with permanent parotid gland and stomach fistulas and with their ureters excluded to the skin surface were studied at an altitude of 2000 to 3100 meters to establish the possible effect of high altitude on the relationship between salivary gland activity and kidney function. The animals were given 500 ml. of water at 36° to 38° C through the stomach fistula. Urine was collected every 15 minutes and saliva specimens were taken every 2 minutes. The kidney-salivary gland function was found to differ at high altitude from that at near-sea level. This difference could be explained by the effect of hypoxia on the central nervous system. Oxygen deficiency led to a disturbance in reflex coordination between digestive functions and others, such as cardiac activity and respiration. As a result, saliva secretion was depressed and urine output increased. Prolonged stay at high altitude led to normalization of these functions.

Esipenko, B. E., and A. P. Kostromina. Kidney function at high altitude. In: Oxygen Deficiency, pp. 446-452. Makarchenko, A. F. (ed.) Kiev: Akademiia Nauk Ukrainskoi SSR, 1963. Kidney function was studied at near-sea level and at altitudes ranging from 2000 to 3200 meters in dogs which were provided with a stomach fistula and had their ureters excluded to the skin surface. The following conclusions were reached: urine volume increased with an increase in altitude; an increase in water intake resulted in an increase in urinary volume at 2000 meters, but at higher altitudes normalization or even a fall below normal was noted; and the amount of solids increased with altitude. However, without forced water intake, it was seen that values were lower than at near-sea levels, and changes in the urine formation process were the result of water equilibrium dynamics under conditions of high altitude, and were directed toward aqueous homeostasis of the organism.

Evans, G. The effect of low atmospheric pressure on the glycogen content of the rat. Amer. J. Physiol. 110:273-277 (1934). It appears that there is a substantial increase in the total carbohydrate of rats when they are without food for 24 hours and at a pressure of 1/2 atmosphere. The greatest increase occurs in the liver and cannot be accounted for by decreases in carbohydrate elsewhere, as would be the case if this phenomenon is due to any hitherto accepted action of epinephrine. All recognized forms of carbohydrate occurring in the body in amounts capable of accounting for such a large increase are themselves found to be increased or undiminished.

F

Febler, J., and J. Banister. Congestive atelectasis in lungs of rabbits and other animals subjected to action of low barometric pressure. Quart. J. Exp. Physiol. 33:291-309 (June 1946). In rabbits, guinea pigs, rats, cats, and a dog subjected to the action of low barometric pressure, congestive lung atelectasis, of varying extent, has been found at postmortem examination. Experiments on rabbits exposed to decreased partial pressures of oxygen at different barometric pressures have shown that there is no relationship between the incidence of congestive atelectasis and partial pressure of oxygen. The animals dying of anoxia at ground level, or at barometric pressures between 500 and 300 mm. Hg, showed all the usual lung changes but no congestive atelectasis. The animals decompressed from 3 or 5 atmospheres pressure to ground level also did not exhibit this lung change. No relation was found between the rate of decompression from the normal to low barometric pressures and the incidence or extent of congestive atelectasis. The animals decompressed from 3 or 5 atmospheres pressure to ground level also did not exhibit this lung change. There was no relation between the rate of decompression from the normal to low barometric pressures and the incidence or extent of congestive atelectasis. A direct relationship between the level of decompression (300 to 900 mm. Hg) and the incidence and extent of atelectasis was formed, and it was concluded that the absolute rarefaction of air was the prime cause of congestive atelectasis formation. An increase of intra-pulmonary pressure maintained in animals at low barometric pressures prevented lung formation. The results of experiments by Hanson and Sjostrand in the formation of lung atelectasis under the influence of different factors decreasing lung capacity at ground level are confirmed. A discussion follows on the possible mechanism responsible for the lung atelectasis formation under the influence of low barometric pressure.

Fenn, W. O. The pressure volume diagram of the breathing mechanism. In respiratory physiology in aviation. Project No. 21-2301-0003, Randolph AFB, Texas (Sept. 1954). The pressure-volume diagram and the methods employed to attain the respiratory data expressed on it have been outlined in detail in a previous paper by the author, American Journal of Medicine 10(1):77-90 (1951). The pressure-volume diagram is based on three types of respiratory measurements: maximum

expiratory and inspiratory pressures at different lung volumes; relaxation pressures at different lung volumes; and, vital capacities, tidal air, and inspiratory and expiratory reserves at different lung pressures. This paper presents a series of curves derived from measurements of subjects who were exposed to the following respiratory situations: pressure breathing; artificial respiration; pneumothorax; and breathing at altitude. In accordance with the experimental conditions, the respective diagrams show the boundaries of the following: air regions, maximum expiratory and inspiratory (vital) capacities, residual air pressures, and pulmonary blood pressures.

Fenn, W.O., H. Rahn, A.B. Otis, and L.E. Chadwick. Physiological observations on hyperventilation at altitude with intermittent pressure breathing by pneumolator. J. Appl. Physiol. 1:773-779 (1949).

Fenn, W.O., H. Rahn, A.B. Otis, and L.E. Chadwick. Voluntary pressure breathing at high altitudes. J. Appl. Physiol. 1:752-772 (May 1949). A study was made of the relative effectiveness of a voluntary increase in the pressure of gases in the lung at the height of

each inspiration as a means of improving the tolerance to high altitude in cases of emergency. The increase in the saturation of the arterial blood which results from this voluntary pressure breathing (UPB) recommended by Commoner is shown to depend chiefly upon the concomitant hyperventilation. Systematic comparisons were made at simulated altitudes (18,000, 25,000, and 42,000 feet) of the relative effectiveness of voluntary pressure breathing, and simple, moderate amounts of hyperventilation. Simultaneous measurements were made of the composition of the alveolar air and the volume of the ventilation.

Fenn, W.O., H. Rahn, and A.B. Otis. Theoretical study of composition of alveolar air at altitude. Amer. J. Physiol. 146:637-653 (Aug. 1946). Equations are developed for calculating the alveolar air composition in terms of the altitude, composition of the inspired air, alveolar ventilation volume, rate of oxygen consumption, and R.Q. These equations are illustrated graphically in a series of charts in which pCO_2 is plotted as ordinates against pO_2 as abscissae. The important physiological consequences of these equations are pointed out. This study presents a theoretical treatment of certain known facts of high-altitude physiology.

Ferro-Luzzi, G., and E. Sorge. Total thyroidectomy in therapy of circulatory insufficiency in Eritrea. Boll. Soc. Ital. Med. Trop. 7:341-378 (1947).

Ferro-Luzzi, G. High altitude and diseases of circulatory system: clinical and experimental study. Boll. Soc. Ital. Med. Trop. 3(1):9-86.

Filstova, L.G. Data on hypoxia and acclimatization. AFSC N65-17817, Foreign Technology Div., Wright-Patterson AFB, Ohio (24 Nov. 1964). A study of the effects of hypoxia on human and animal organisms in the Kirgizia region, at 760- to 2500-meter altitude did not disclose a basic mechanism of adaptation. Both animals and men showed a lowering of the energy expenditure level and it is possible that the thyroid gland may play a role in this mechanism. The extero-receptors (vision, hearing, and smell) may also take part in adaptation since the exclusion of these receptors resulted in an increase of hypoxia tolerance.

Finkelstein, B., and R.G. Pippitt. Effect of altitude and oxygen upon primary taste perception. J. Aviation Med. 29(5):386-391 (May 1958).

Fiorioli, W. Roentgenological studies on the action of stomach tonus during adaptation to altitude. Med. Klin. (Berlin) 52(43):1879-1881 (25 Oct. 1957).

Fiorioli, W. X-ray investigation of the behavior of gastric tonus during adaptation to altitude. Med. Klin. 52(43):1879-1881 (Oct. 1957). Investigations of gastric peristalsis were undertaken in 51 subjects during a one- to two-week skiing course at Obergurgl (2000 meters altitude). Orthodiagraphic observations of the gastric shape and peristalsis movements were carried out before eating, in the morning and at noon. In most subjects there was a decrease of the gastric tonus and a lengthening of time intervals between the peristaltic waves by approximately 6 seconds. Of the 14 cases without changes in the gastric tonus, eight had primary hypotonicity.

Fiset, P. E., and L. D. Dugal. Sensitivity of man to oxygen deficiencies corresponding with 10,000-foot altitude; preliminary report. Rev. Canad. Biol. 8:257-261 (1949).

Fishman, A. P. Pulmonary vascular and circulatory responses to acute hypoxia. Presented at Fifth Annual Conference on Research in Emphysema: Normal and Abnormal Pulmonary Circulation.

Med. Thorac. 19(5):438-448, 1962. The argument is developed that both pre-capillary hypoxemia and post-capillary hypoxemia may elicit pulmonary vasoconstriction by direct effect of the hypoxic blood on the respective vascular segments. The affected segment varies with the route by which hypoxemia is induced. By way of contrast, acute hypercapnia appears to be without apparent effect on the pulmonary circulation. Acute acidosis constitutes an independent stimulus for pulmonary vasoconstriction. Effects previously attributed to acute hypercapnia seem to operate through the associated acidosis.

Fishman, A. P., and H. W. Fritts, and A. Cournaud. Effects of acute hypoxia and exercise on the pulmonary circulation. Circulation 22(2):204-215 (1960). The effects of acute hypoxia and of graded exercise on the pulmonary circulation were studied in 17 normal subjects. The contrasting effect of both these stimuli on the pulmonary artery pressures were striking: namely, the significant increase in pulmonary arterial pressure with a minimal rise in cardiac output during acute hypoxia, and the small pulmonary arterial pressure rise with with a large increase in cardiac output during exercise. Surgical resection of the preganglionic fibers and ganglia which supply sympathetic efferent nerves to the pulmonary vessels was without effect on the response of the pulmonary circulation to both stimuli.

Fitzgerald, O., M.F. Mason, and F. Vergon. Changes in serum bilirubin and erythrocyte count in high-mountain region. Helv. Med. Acta (supp. 5) 7:50-57 (1940).

Fleisch, A., and E. Grandjean. Tonus of skeletal musculature in high-altitude climate. Helv. Physiol. Pharmacol. Acta 6:474-483 (1948).

Flekkel, A.B. Effect of thin atmosphere on color sensitivity in various states of color vision. Voennomed Zh. 5:32-35 (May 1959).

Flückiger, E., and F. Vezar. Persistence of adaptation to low-atmospheric pressure demonstrated on heat regulation. Helv. Physiol. Pharmocol. Acta 11:67-72 (1953).

Flückiger, E. The oxygen consumption of the rat exposed to lowered oxygen partial pressure. Helv. Physiol. Pharmocol. 14(3):369-381 (1956). The significance of chemical thermoregulation in the decline in body temperature associated with hypoxia was investigated in rats. Measurement of oxygen consumption was made during 10-percent O_2 breathing (at atmospheric pressure) before, during, and after exposure for a period of 2 weeks to an ambient air pressure of 350 mm. Hg. The oxygen consumption of normal rats decreased to

a maximum of 30 percent within 15 minutes after initiation of 10-percent O_2 breathing. Rectal temperatures decreased gradually throughout several hours of hypoxia. After two weeks, rats previously exposed to altitude showed a gradual increase in oxygen consumption to a value approaching normal during 10-percent O_2 breathing. The metabolic adaptation to hypoxia in these animals was observed for 8 days after return to normal ambient pressure. Rectal temperature during continuous exposure to lowered ambient pressure was restored to normal within 3 to 4 days. It is concluded that the decrease in body temperature observed during hypoxia is the result of decreased oxygen consumption, and that the restoration of rectal temperature during prolonged hypoxia is accomplished chiefly by physical heat regulation.

Flückiger, E., and F. Velzar. Lowering and restitution of body temperatures at low atmospheric pressure and the effect of thyroid and pituitary and adrenal cortex on it. Helv. Physiol. Pharmocol. 10(3):349-359 (1952). Rats exposed to low atmospheric pressures (350 mm. Hg) and low temperature (22 to 23°C) showed a drop of body temperatures (4 to 5° C in about 3 to 4 hours), which was restored to normal in about two days of continuing exposure. When the animals, were returned to atmospheric pressure, after restoration of the body temperature to normal, their body temperature rose 1 to 1.5° C above normal for a few days. If the surrounding temperature at low pressure was 27 to 29° C, no abnormal body temperature changes were observed. However, a group of thyroidectomized animals showed lower body temperatures even under these latter conditions. Adrenalectomized or hypophysectomized rats restored their body temperature upon return to normal pressure only incompletely, or not at all. The physiological mechanisms of the observed phenomena are discussed.

Flückiger, E., and F. Vezar. Lack of adaptation to low oxygen pressure in aged animals. J. Geront. 10(3):306-311 (July 1955). Adaptation to low atmospheric pressure of 350 mm. Hg was studied in 64 male rats between the ages of 45 to 570 days (2 to 20 months). Adaptation was tested by the decrease and restoration of body temperature during 15 days of continuous exposure to low atmospheric temperature. Retained adaptation was also tested after an additional study of 40 hours at normal barometric pressure (732 mm. Hg at Basel). Fourteen- to twenty-month-old rats were completely unable to restore the normal body temperature after the initial drop during the first few hours of exposure to low barometric pressure. They also showed a decreased

retained adaptation in contrast to the findings in younger animals. There was no significant difference in the increase of blood hemoglobin between young and old rats in response to a ten- to fifteen-day exposure to 350 mm. Hg.

Flugge, C. Climatic observations in high and middle altitudes. Z. Tuberk 37:1-13 (Oct. 1922).

Foa, A. Comparative research on capillary resistance and on blood platelets of children living in plains and of those living in mountain regions. Pediatric Med. Prat. 9:301-309 (May 1934).

Foa, C. Bioclimatic study in Brazilian mountains. Resen. Clinicocient 12:183-187 (1 May 1943).

Foldi, M., F. Solti, and E. Koltay. Effect of hypoxia on kidney function in patients with renal disease. Acta Med. Acad. Sci. Hung. 10(3):335-338 (1957). In patients with renal disease, arterial hypoxia induced by breathing of an O_2-N_2 mixture does not lead to characteristic changes in the renal function. In normal subjects exposed to hypoxia, diuresis decreased to 50 percent of the initial volume, sodium excretion to 57 percent, glomerular filtration rate to 52 percent, and the effective renal plasma flow to 34 percent of the initial average values.

Forbes, W.H. Blood sugar and glucose tolerance at high altitudes. Amer. J. Physiol. 2:309 (July 1936). Determinations were made of the amount of sugar in the blood of acclimatized subjects in rest and work at various altitudes up to 6140 meters. Glucose tolerance tests were given at 5340 meters. In rest, the blood sugar rose slightly with altitude, but it is not certain whether this can be attributed to the altitude. The behavior of the blood sugar in work was approximately the same at all altitudes. The glucose tolerance was greatly increased at 5340 meters in two subjects, and changed (though not increased) in a third who had an abnormal tolerance curve at sea level.

Forchu-Mayr, O. Investigations concerning the leukocyte picture and the reticulocytes. Wien. Z. Inn. Med. 33(6):220-223. Percentual variations of leukocytes and reticulocytes were determined in the blood of 23 participants of a course in alpine sports, offered by the Institute of Physical Education of the University of Innsbruck, during and after physical training at an altitude of 2860 meters. After acclimatization to the altitude, a slight increase in reticulocytes was observed when the training was stepped up. There was also a slight "shift to the left" (preponderance of young neutrophils) which persisted after return to the plain. Where altitude acclimatization was incomplete, excessive training and accumulated fatigue caused a marked increase in reticulocytes, a decrease of lymphocytes, and again, a slight shift to the left. Where training was lacking and acclimatization had not been completed, a conspicuous increase of reticulocytes and a distinct shift to the left, but no incidence of leukocytosis were observed.

Forchu-Mayr, O. On respiration in high mountains while carrying various loads. Wien. Klin. Wschr. 65(8):160-161(1953). The vital pulmonary capacity was determined on student athletes during a 10-day hike to altitudes of 2860 and 3248 meters while carrying various loads (up to 15 kg.). During the first 3 days at high altitude, vital capacity decreased, then rose again, with a tendency to drop back because of increasing fatigue. Upon return to the plain, vital capacity values were higher than at the start, but only in 45 percent of the subjects. Because the exercise was too strenuous even for athletes, and the duration of the experiment was too short, altitude acclimatization could not take effect.

Forchu-Mayr, O., and G. Biedermann. Cardiovascular tests following ski racing in high mountains for 23 km. Munchen Med. Wschr. 96:134-135 (5 Feb. 1954) and 166-169 (12 Feb. 1954).

Fossan, D. D., E. E. Baird, J. D. Julian, and J. A. Webb. Evaluation of the postmortem test for hypoxia in the human. School of Aerospace Med., Report No. 61-55, AF Aerospace Med. Center, Brooks AFB, Texas (May 1961). In previous investigations, a simple postmortem test for determining ante-mortem hypoxia was developed and successfully proved on animals. The test is based on the fact that lactic acid accumulates in brain tissue of animals made hypoxic at the time of death. This study tries to determine whether or not the elevated postmortem level of lactic acid is associated with a history of clinical hypoxia with sufficient consistency to warrant its use as a diagnostic test in man. The biochemical and physiologic mechanisms involved in the test are explained. Analyses of lactic acid in brain tissue were performed on 168 autopsied patients; clinical histories of the patients were recorded with special emphasis placed on the state of oxygenation of the tissues immediately ante-mortem.

Fossan, D. D., and C. Biddulph. Effect of altitude and of anesthesia on brain electrolytes and lactic acid. Amer. J. Physiol. 196(5):1063-1066 (May 1959). The concentration of lactic acid, sodium, potassium, and calcium was measured in four structures of the brain 3 hours after death in anesthetized and unanesthetized dogs which had been subjected to simulated altitude and ground level control protocols for 15 minutes. The effect of the simulated altitude was elevation of the sodium concentration in the corona radiata but not in the cerebral cortex or caudate nucleus; the calcium concentration in the cortex, corona radiata and caudate nucleus; and the lactic acid concentrations in all the tissues. No potassium changes were noted. The effect of the anesthesia was very slight and only indirectly detectable. The sampling problem was studied and caudate nucleus and cortex recommended as sampling sites for the detection of hypoxia by lactic acid elevation if a whole hemisphere cannot be used. It is pointed out that accuracy in diagnosing acute mortem hypoxia depends upon discrete anatomical sampling since lactic acid is not evenly distributed within the brain. A chemical approach is presented, which gives compensation for the uneven distribution of lactic acid.

Fowler, K. T., and John Reed. Effect of alveolar hypoxia on zonal distribution of pulmonary blood flow. J. Appl. Physiol. 18(2):244-250 (1963). Redistribution of pulmonary blood flow was studied by means of the cardiogenic oscillations of expired gas tensions in six normal subjects after induction of alveolar hypoxia (13.5 percent inspired O_2). In three subjects the upper zones of the lungs were

found to receive a considerably greater proportion of total pulmonary blood flow during hypoxia in both vertical and horizontal postures. Two subjects showed no redistribution in either position. The response of one subject was intermediate between these two groups. It is concluded that there is no pulmonary vascular response to alveolar hypoxia in some subjects; in others, there is a response consisting of preferential lower-zone vasoconstriction of greater or lesser magnitude. Earlier data on the effects of hypoxia on the pulmonary circulation are shown to be consistent with the operation of this mechanism.

Francois - Franck, C. A. Etudes de quelques arrets respiratoires. Apnee. Phenomene de Cheyne - Stokes. J. Anat. Physiol. 13:545-570 (1877).

Frawley, T. F., M. Roche, D. Jenkins, and G. W. Thorn. The role of the pituitary adrenocortical system in the response to anoxia. J. Clin. Invest. 30:638 (1951).

Fred, H. L., A. M. Schmidt, L. Bates and H. H. Hecht. Acute pulmonary edema of altitude: clinical and physiologic observations. Circulation 25(6):929-937 (June 1962). Three separate episodes of acute pulmonary edema that developed in two otherwise healthy individuals during heavy exertion at high altitudes are described. Detailed physical examination and laboratory studies failed to demonstrate pulmonary infection or cardiac disease. Data obtained by cardiac catheterization during one of these episodes revealed elevation of the pulmonary artery pressure and a normal left arterial pressure. This syndrome appears to be the consequence of pulmonary vascular obstruction distal to the capillary bed, presumably in the pulmonary veins. It is brought about by exposure of susceptible individual to high altitudes, and is completely reversed by oxygen administration.

Fregly, M. J. Effect of chronic exposure to hypoxia on blood pressure and thyroid function of hypertensive rats, SAM-TDR-62-96, (March 1963). Chronic exposure to an atmosphere containing 13-percent oxygen protects against development of renal hypertension in rats. The mechanism through which the rats are protected may involve the thyroid gland since certain criteria for assessment of thyroid function, using radioactive iodide, suggest depression of activity. Other physiologic mechanisms, brought into play as a result of hypoxia, may also contribute and need to be studied.

Frehn, J. L., and A. Anthony. Respiration of liver slices from normal and altitude-acclimatized rats. Amer. J. Physiol. 200 (3):527-529

(March 1961). Analyses were made of the respiratory rates of liver tissue slices from normal rats and from rats continuously exposed to simulated altitudes of 21,000 feet for periods varying from 1 to 56 days. Seventy-one rats were used. The O_2 uptake was measured in 100, 20 and 1 percent O_2. There was no difference in tissue respiration between the control and experimental animals, either with no added substrate and with glucose or succinate as added substrates. It was concluded from these data that alterations in cellular respiration do not constitute an important feature of altitude acclimatization.

Frenkel - Tissot, H.C. Blood at high altitude. Schweiz. Med. Wachr. 52:613-617 (15 June 1922).

Frey, J., and H. Jochmann. Behavior of red bone marrow in hypoxemia (in high-mountain climate). Klin. Wschr. 26:728-729 (1 Dec. 1948).

Freydberg, H. Basal metabolism in medium altitudes. Schweiz. Med. Wschr. 86(21):629-630 (26 May 1956). The basal metabolic rate (BMR) was measured in 5 subjects at altitudes of 270 meters (Basel), 1770 meters (St. Moritz-Bad), and 3026 meters (Piz Nair). There was no significant increase in the BMR for any of the subjects at the 1770-meter altitude. Only one subject had a significantly elevated BMR at 3028 meters.

Friedemann, T.E. Work at high altitude: effect of diet and other factors in use of lactic and pyruvic acids, and lactate - pyruvate ratio in human subjects at simulated high altitudes. Quart. Bull. Northwest. Univ. Med. Sch. 23:448-455 (1949).

Friedemann, T.E., and A.C. Ivy. Work at high altitude: plan of study and methods. Quart. Bull. Northwest. Univ. Med. Sch. 21: 31-44 - (1947). Although acclimatization may increase the ceiling to altitude or the tolerance to anoxia, it is a slow process and cannot be applied practically to the aviator, the air-borne passenger, or to troops that are forced to maneuver at elevated altitudes; its effects soon pass after return to more normal altitudes. How can efficiency be increased and an adequate function maintained? These are fundamental problems in medicine, biochemistry and nutrition and apply generally to such diverse conditions as cardiac or respiratory failure, anemia, surgical shock, and exhausting physical exercise in which varying degrees of organic failure contribute to tissue anoxia in spite of a rich supply of atmospheric oxygen.

Friedemann, T.E. Work at high altitudes: Utilization of thiamine and riboflavin in low- and high-dietary intake: effect of work and rest. Quart. Bull., Northwest. Univ. Med. Sch. 23:177-197 (1949).

Friedemann, T.E., A.C. Ivy, B.B. Sheft, and V.R. Kinney. Work at high altitudes; relation between daily oral intake and excretion of thiamine and riboflavin. Quart. Bull., Northwest. Univ. Med. Sch. 23:438-447 (1949).

Friedemann, T.E. Production of lactic and pyruvic acids during work at ground level and at increasing altitude to 15,000 feet. Quart. Bull., Northwest. Univ. Med. Sch. 21:228-237 (1947).

Fritts, H.W., E. Braunwald, A.P. Fishman, and A. Cournand. Influence of induced hypoxia on the central blood volume of normal man. Fed. Proc. 15:68 (1956).

Fritz, G. Physiology of climate of high altitudes; effect of decreased atmospheric pressure on pH and on carbon dioxide binding power of blood. Biochem. Z. 170:236-243 (1926).

Fronius, H. Respiration and metabolism of trained and untrained persons in high-altitude flights. Arbeitsphysiol. 7:44-61 (1933).

Fryers, G.R. Effect of decreased atmospheric pressure on blood volume of rats. Amer. J. Physiol. 171(2):459-464 (1952). Eight groups of rats were exposed to a simulated altitude of 15,000 feet for

durations of 3 to 100 days. One group was maintained at 15,000 for 35 days and then raised to 20,000 feet for an additional 13 days. The total red cell volume showed a pronounced increase during the initial time of exposure, while the plasma volume decreased at an equal rate. Hemoglobin values per 100 gram increased steadily with increasing altitude, but leveled off at about 20,000 feet.

Fudel-Osipova, S.I., and F.I. Grishko. An early indicator of the adaptive reaction of muscle tissue to develop senescent hypoxia. AFSC 65-17765, Foreign Technology Div., Wright-Patterson AFB, Ohio. Experiments on rats of different ages, ranging from 1 day to 37 months, showed that 15-month-old rats have the highest rate of tissue respiration. At 37 months, the respiration had dropped by almost 50 percent. The decline in tissue respiration in older animals may depend upon a decrease in active substrate and a decrease in enzyme activity. Microscopic examination of muscle fibers showed that fiber thickness was smaller in the older animals. Also, it was observed that while the majority of cells in the aged have lost their ability to divide, the nuclei begin to divide at a higher rate. It was concluded that the appearance of a large number of nuclei indicates oxygen starvation and that oxygen consumption by the tissue diminishes with age. The appearance of a large number of nuclei serves as an early criteria of aging and the onset of tissue hypoxia.

Fumagalli, G., and M. Mezzano. Respiration during acute hypoxia in the normal subject: critical analysis. Rev. Med. Aero. (Rome), 20(2):235-248 (Apr.-June 1957). Normal subjects at rest breathing a gas mixture containing 11.2 percent of oxygen showed changes in pulmonary ventilation; however, these changes did not modify the condition of the compensating respiratory response. Electrocardiographic tracings in this group exhibited no changes. Under the same conditions, breathing a mixture of 8.63 percent of oxygen caused greater changes in pulmonary ventilation and a hypoxic state close to the limits of tolerance; and in 4 out of 6 cases, electrocardiographic changes.

Fumagalli, G., and M. Mezzano. Effect of diphosphopyridine nucleotide on respiration during acute hypoxia. Rev. Med. Aero. (Rome) 20(4): 644-675 (Oct.-Dec. 1957). Young subjects were given diphosphopyridine nucleotide (DPN) [NAD] intravenously, and subjected to hypoxia. In comparison with previous research in which cocarboxylase was used, the following factors were found: a decrease in oxygen consumption during the first six minutes of the experiment, less marked than when cocarboxylase was administered; a remarkable increase in oxygen consumption after 30 minutes, attaining higher values than those observed in simple hypoxia; a high increase in the respiratory quotient after 6 minutes, followed by a decrease after 30 minutes, due chiefly to increased oxygen consumption; and, a lower intensity of electrocardiographic signs indicating lower myocardial cell motility in response to hypoxic stimulation. DPN provides higher resistance to hypoxia and better protection to the myocardium than does cocarboxylase.

Fumagalli, G., and M. Mezzano. The effects of cocarboxylase on respiration during acute hypoxia. Rev. Med. Aero. (Rome) 20(4):619-631 (Oct.-Dec. 1957). Cocarboxylase was administered intravenously to six subjects between 16 and 25 years of age who then breathed a hypoxic mixture (8.6 percent oxygen). A decrease in oxygen consumption was observed during the first 6 minutes of the experiment along with an increase in the respiratory quotient which lasted until the end of the 30-minute experiment. Several electrocardiographic changes were also found. Cocarboxylase appears to provide the body with a better tolerance to acute hypoxia, as indicated by the respiratory adaptation to hypoxic stress and the utilization of oxygen at the tissue level.

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Gabl, F., and M. J. Halhuber. Adrenocortical activity in high mountain climate. Wien. Z. Inn. Med. 43(5):217-222 (May 1962).

Observation of urinary cortisone excretion and the red blood count in studies conducted with five subjects during 4 weeks in a high-mountain resort at 2000-meter altitude showed a statistically significant increase of the adrenal cortex activity in the first week, which receded in the second week, followed by marked fluctuations in the third week, and in the fourth week finally returning to the initial values (preliminary values obtained at sea level). These results are in agreement with the findings from investigations of different organs and systems which tends to the conclusion that there is a nonspecific adaptation process which subsides only in the fourth week after proceeding on a stepwise course.

Gallenga, R. Effect of fatigue in high-mountain climate on size of pupil. Rass. Ital. d'ottal. 1:263-270 (Mar.-Apr. 1932).

Gambaa, P. D., J. Dyer, M. Echivararria, and E. Marticorena. The influence of high altitudes on the electrical activity of the heart:

electrocardiographic and vectorcardiographic observations in the newborn, infants, and children. AF School of Aviation Med., Report No. 60-79, Randolph AFB, Texas (1960).

Gaudelsman, A. V., R. P. Gracheva, and N. V. Prokopovich. Adaptation of man to hypoxemia during muscular activity. Fiziol Zh. SSSR 46(7):989-999 (1960). Adaptation to hypoxemia develops in athletes in the course of many years' training in prolonged and intensive motor tasks. This is revealed in a remarkable capacity for the performance of prolonged motor activities when the level of oxygen saturation of the blood is markedly reduced and fluctuates widely. In the trained athlete, in contrast to the untrained subjects, the amplitude and frequency of the action potential in the skeletal muscles during intensive muscular activity were unchanged during the period of pronounced hypoxemia. There was also little change in the amplitude of the ECG spikes. These findings can be explained by the development in the training process of great resistance to hypoxemia in the nerve centers of athletes, and possibly also in the muscle tissues. An essential feature in adaptation to hypoxemia in motor activity is the simultaneous adaptation to hypercapnia. It is possible that this combination, by increasing the resistance of nerve centers

to deficiency of oxygen and intensifying the utilization of oxygen by the tissues, is of adaptational significance. Hypoxemia during intensive and prolonged motor activity in trained athletes was not the result of inadequacy of external respiration. Any compensatory increase of pulmonary ventilation during motor activity was very feeble and voluntary intensification of respiration did not eliminate the hypoxemia. Circulatory functional readjustment would appear to be the basis of the adaptation to deficiency of oxygen in athletes. Adaptation to hypoxemia with simultaneous hypercapnia constitutes an important feature of prolonged and intensive motor training.

Ganoza, R. P. Anesthesia at altitude. Rev. Asoc. Med. de la Provincia de Yauli (La Oroya) 5 (1-4):143-147 (Jan.-Dec. 1960). Since persons living at high altitudes exhibit hypotension, a normal or bradycardic pulse, and a reduced basal metabolic rate, the use of potentiated anesthesia for surgical procedures with ganglioplegic drugs (which reduce metabolism) causes reactions different from surgical patients at sea level. Excellent results are obtained at altitudes with a mixture of largactil phenergan and demerol administered one hour prior to surgery. Nitrous oxide anesthesia is not suitable for use at altitude.

Garcia-Godos, R. M. Influence of position of body on pulse and arterial pressure as observed at sea level and at high altitude. An. Fac. Med. (Lima) 28:101-123 (1945).

Garcia, J. F. Erythropoietic response to hypoxia as a function of age in the normal male rat. Amer. J. Physiol. 190(1):25-30 (July 1957). Rats 5 to 250 days of age were exposed to a hypoxic environment (9.0-percent oxygen) 6 hours a day for 14 days, and red cell volumes were determined by the measurement of injected Fe^{59}. During the growing period of 5 to 30 days, the rats showed no significant change in blood production under the hypoxic stimulus. Rats 50 days of age were the youngest group to show a marked increase in total blood-cell volume and total hemoglobin counts. It is suggested that blood-cell production in the young rats is at the maximum value and the hypoxic stimulus does not tend to increase the production.

Gardinghi, G., and F. Giaccai. Stenosis of trachea: modifications of intratracheal pressure in stenosis due to various altitudes; experimental study. Otorinolaring. Ital. 17:352-358 (1948).

Garrido-Kling, G., and L. Pena. The gastroduodenal ulcer in high altitudes (Peruvian Andes). Gastroenterology 37 (4):390-400 (1959).

The general incidence of gastroduodenal ulcer in a group of 17,500 insured laborers (chiefly miners) born and living in the Peruvian Andes (between 10,000 and 16,000 feet above sea level) was 0.4 percent. The relation of gastric to duodenal ulcer was 20.6:1. The greatest incidence of gastric ulcer occurred in the group between 21 and 30 years of age. There were hemorrhages in 66 percent of the cases. A greater predisposition to suffer from gastric ulcer appeared to exist in the Andean nations. In high altitudes, the vascular and hematic factors, as well as chronic stress, play important roles in the etiopathogenesis of gastric ulcers.

Garsaux, B., and C. Ricket. Experimental reproduction of mountain sickness. C. R. Soc. Biol. (Paris) 96:768-770, (25 Mar. 1927).

Gasenko, G. G., and N. P. Blagovestova. Regeneration of erythrocytes in high mountain climate: inaccuracy of staining reaction due to effects of radiant energy on stain. Bull. Biol. Med. Exper. URSS 9:130-132 (1940).

Gaspa, P. H. Changes in the hepatic glycogen level at simulated altitude. Med. Aero. (Paris) 7 (4):471-475 (1952). Literature data on the changes in the glycogen content of the liver in animals exposed

to simulated altitudes are contradictory; some authors have reported increases, others decreases of the glycogen level. The author made exact measurements of the glycogen content of the liver tissues of guinea pigs both exposed to altitude and unexposed controls. The glycogen level was found to be augmented in the decompressed animals. It is concluded that both the increased liver glycogen and the simultaneous hyperglycemia may be caused by a diminution of organic oxidation at low ambient pressure.

Gasparian, N. A. Effect of hot climatic conditions in the city Erevan and of mountain climatic factors on chronic dysentery in children. Zh. Mikrobiol. 30:73-78 (Aug. 1959).

Gaudy, J. P., and R. Stämpfi. Electric conductivity of blood and blood plasma in high-mountain climate: relation to erythrocyte content and erythrocyte volume. Helv. Physiol. Pharmacol. Acta 6:674-687 (1948).

Gellharn, E. Oxygen deficiency, carbon dioxide and temperature regulation. Amer. J. Physiol. i:190-194 (Sept. 1937). The loss of body temperature resulting from inhalation of gas mixtures with low-oxygen tension is greatest and develops most rapidly in animals with relatively large surface area (mice). Under conditions of oxygen deficiency, 3-percent CO_2 in the inhaled air increases the fall in body temperatures over that observed in oxygen deficiency alone. The fact that the fall of body temperatures is greatest under these conditions, although the oxgenation of the tissues is improved, indicates that the fall in body temperature is not regulated exclusively by the oxygenation of the tissues, but that the specific influence of CO_2 on the circulatory system plays an important part in increasing the heat release from the surface of the body.

Gellhorn, E., and H. Haulman. The effect of anoxia on sense organs. Fed. Proc. 2:122-126 (1943).

Gellhorn, E., and A. Janus. The influence of partial pressures of O_2 on body temperatures. Amer. J. Physiol. 2:327-329 (July 1936). Three groups of experiments are reported in which guinea pigs were subjected to: (1) a lowered barometric pressure, normal air being used so that atmospheric pressure and partial pressure of O_2 were diminished; (2) a reduction in the partial pressure of O_2 at normal barometric pressure; and (3) a reduction of barometric pressure at normal partial pressures of O_2. The temperature remained normal in (3) and was lower in (\`\` and (2) to the same degree, thereby showing that the partial pressure of O_2 influences the body temperature and that alterations in the barometric pressure are without any effect.

Gemmill, C. L., E. M. Gerling, and D. L. Reeves. The respiratory effect of prolonged anoxemia in normal dogs before and after denervation of the carotid sinuses. Amer. J. Physiol. 709 (4):713 (Oct. 1934). A study was made of the respiratory responses of four normal dogs before carotid sinus denervation and of two dogs after denervation to pure nitrogen to gas mixtures of 14.5, 9.5 and 5.1 percent oxvgen in nitrogen, and to cyanide injections.

Gemmill, C. L. Acclimatization: review of physiologic observations. U.S. Naval Med. Bull. 39:178-187 (Apr. 1941).

Gerard, R. W. The response of nerve to oxygen lack. Amer. J. Physiol. 2:498-541 (Mar. 1930).

Gerathewohl, S. J. Study of acclimatization during a two-week exposure to moderate altitude. J. Aviation Med. 25 (2):156-163 (Apr. 1954). Complex reaction experiments were made at ground level (761 feet) and at moderate altitude (10,152 feet) in order to study the effects of mild hypoxia on psychomotor performance, and to find if acclimatization occurs during a period of thirteen days. The group mean scores of correct responses obtained at the first four altitude tests were consistently lower than the mean scores of the last three pre-altitude tests. The statistical analysis yielded large variations between individual curves, and revealed characteristic differences in sensitivity to hypoxia. Two of the nine subjects showed a pronounced loss in performance during the whole altitude period. Seven out of the nine test subjects became acclimatized within a period of thirteen days.

Gesell, R., H. Krueger, G. Gurham, and T. Bernthal. The regulation of respiration. Amer. J. Physiol. 2:300-338. A study was made of tidal air, pulmonary ventilation, respiratory movements, carbon dioxide and oxygen content of expired air, total elimination of carbon dioxide and total absorption of oxygen, expiratory quotient, lactic acid content of the blood, carbon dioxide capacity of the blood, hydrogen ion concentration of the blood, volume flow of blood, mean arterial blood pressure, oxidative energy, and non-oxidative energy. The following relationships were also studied: shortages of oxygen consumption to accumulated lactic acid, excess oxygen consumption to the disappearance of lactic acid, total elimination of carbon dioxide to that required by oxidations, the lactic acid content of the body to the liberation and retention of carbon dioxide. The proportion of fixed acid combining with bicarbonate and that reacting with other buffer systems was investigated.

Ghinozzi, G.P., and G. Meiner. Behavior of diuresis in subjects exposed to simulated altitudes of 3400 meters (BP = 493 mm. Hg) and 4500 meters (BP - 433 mm Hg). Rev. Med. Aero. (Rome) 20 (1):76-81 (Jan.-Mar. 1957) Eight males subjected to mild anoxic anoxia at simulated altitudes of 3500 and 4500 meters respectively showed an increase in diuresis with a decrease of specific gravity of the urine. Simultaneously an increase in the urinary excretion of bases appeared, possibly related to the increased pulmonary elimination of carbon dioxide.

Ghose, K. Physiological compensatory mechanisms at altitude. Aero. Med. Soc. J. (New Delhi) 1(2):18-27 (Oct. 1954). This is essentially a critical review of the literature dealing with the effects of anoxia on the human organism. Physical aspects of respiratory gaseous exchange are discussed. Compensatory mechanisms which follow the onset of hyperventilation at altitude are described. Hematological changes at altitude are discussed in detail, with particular reference to contradictory reports of experimental data.

Giaja, J. Atmospheric pressure and biological adaptation. Acta Physiol. Pharmacol. (Amsterdam) 5(4):479-486 (Oct. 1957).

Gianotti, M., and S. Goldberger. Gastric secretions after fatigue at altitude. Arch. Fisiol. 30:32-50 (1 Aug. 1931).

Gibbs, F. A., E. L. Gibbs, and W. G. Lennox. Electroencephalographic response to overventilation and its relation to age. J. Pediat. 23:497-505 (1943).

Gibbs, F. A., W. G. Lennox, L. F. Sims, and E. L. Gibbs. Differentiation of the effects of low oxygen and low carbon dioxide on the electrical activity of the cortex. Fed. Proc. 50:129 (1942).

Gibbs, F. A., H. Maxwell, and E. L. Gibbs. Volume flow of blood through the human brain. Arch. Neurol. (Chicago) 57:137-144 (1947).

Gil, J. R., and D. Gonzalez Leran. Macrocytosis of plateaus: importance for correct interpretation of humatic study of patients; hematologic constants in 200 normal persons in Mexico, D.F. Rev. Invest. Clin. 1:71-98 (Oct. 1948).

Gil, J. R., and D. G. Leran. Determination of number of erythocytes, volume of packed red cells, hemoglobin and other hematologic standards in Mexico City (altitude 7457 feet): study made on 200 healthy persons. Blood 3:660-681 (June 1948). (1) Careful studies of the red blood cells in long-time residents of Mexico City (2,273 meters, 7457 feet) show a slight, although definite increase in red cell count. (2) The percentage volume of packed red blood cells, mean corpuscular diameter and the amount of hemoglobin per 100 cc. of blood are higher in Mexico City than at sea level. (3) There is an increase in the MCV and in the MCH as a result of the increase in the hematocrit and in the amount of hemoglobin without a definite correlated hyperglobulin. (4) The MCHC corresponds to the normal values found by other investigators at different altitudes.
(5) The relation between the hematologic standards studied and factors such as age, sex, diet and body build are in agreement with the findings of other workers. The changes mentioned in (2) and (3) have been observed by other investigators working under the same experimental conditions and they differ from those found among temporary residents at high altitudes. It is reasonable to assume that the increase of the MCV and the amount of hemoglobin are the result of a permanent physiologic process of adaptation to high

altitudes, which appears only after a long residence. The existence of macrocytosis with increased corpuscular hemoglobin found above sea level possibly favors a better tissue oxygenation as well as other gaseous interchanges.

Giragossinty, G., and E. S. Sundstroem. Cortico adrenal insufficiency in rats under reduced pressure. Proc. Soc. Exp. Biol. Med. 36:432-434 (1937).

Girling, F., and F. A. Sonahara. An effect of reduced barometric pressure on peripheral circulation. Canad. J. Biochem. Physiol. 35:777-784 (1957). Several groups of investigators have noted in the past that exposure to a reduced barometric pressure results in a decrease in periphal blood blow. In the present study, human subjects were exposed to a pressure of 225 mm. Hg with maintenance of arterial oxygen saturation. The forearm and hand blood-flows were measured plethysmographically. Forearm blood-flow was not affected by the exposure whereas hand blood-flow was reduced in all subjects. Blood pressure and heart rate were also measured and showed no change during the experiment.

Girling, L., and C. Maheux. Peripheral circulation and simulated altitude. J. Aviation Med. 23(3):216-217, 270 (1952). Rabbits were taken to an altitude of 30,000 feet in a decompression chamber without added oxygen. Blood pressure, critical closing pressure, flow, and flow resistance of the femoral artery were measured at 10,000, 20,000, and 30,000 feet during both ascent and descent. No significant changes in blood pressure were noted but there was a considerable (100 percent) increase in resistance to flow. In the second series of tests, the animals were decompressed while breathing 100-percent oxygen. At an altitude of 40,000 feet, they showed no signs of anoxia (but abdominal distention became apparent above 35,000 feet). There was an increased resistance to blood flow at altitude. This was not due to anoxia, as an increased resistance was apparent hether the animals were breathing 100-percent oxygen or not.

Glenn, W. G. Preliminary study of human serum in subjects exposed to simulated altitude. Aerospace Med. 30(8):576-579 (Aug. 1959). Disproportionate changes in the concentration of substances associated with homologous albumin precipitin reactions in agar columns have been found in repeated serum samples from two men constantly

exposed for eight days to simulated altitudes from 10,000 to 17,000 feet. The concentration changes of the albumin components were not in the same direction or of the same magnitude for the chamber partners. One subject showed other serologic evidences of a stressing condition by changes in globulin(s) level and certain carbohydrate protein factors (glycoproteins; namely, mucoprotein and C-reactive protein). The serum samples obtained before and 14 days after the injection of human serum albumin tagged with I^{131}, seemed to indicate that this substance is antigenic in the homologous species. The possibility exists that the exposure to altitude increased the sensitivity of the subjects to a usually compatible albumin.

Gnecco-Mozo, F. Work of heart in Bogota. Rev. Med. (Bogota). 46:49-62 (July-Aug. 1936).

Goggio, A. F., and G. H. Horick. Physiologic abnormalities and pathologic changes following exposure to simulated high altitude. War Med. 7:152 (1945).

Gois, N. Influence of variations of atmospheric pressure on the pilot. Rev. Port. Med. Milit. 8:27-31 (1960).

Gökhan, N., and M. Terzioglu. Leukocytes and leukocyte count at 1850 meters of altitude. Minerva Med. (Torino) 47(53):16-18 (4 July 1956). The leukocyte count in young subjects staying at Uludag, Turkey (altitude, 1850 meters) did not vary significantly outside of normal limits with the exception of a slight increase in young neutrophils and a more notable increase in monocytes. These latter changes were dependent on the stimulative effect of altitude on the myeloid system. Since neutrophils and monocytes have the special function of protecting the body against infection, it is concluded that persons at high altitude are poorly equipped to fight infections in general.

Gold, .. ., J. Q. Barry, and F. P. Ferguson. Early effect of moderate altitude stress on plasma potassium in the dog. J. Appl. Physiol. 15:37-39 (Jan. 1960). Exposure of dogs to a simulated altitude of 30,000 feet for 30 minutes resulted in marked respiratory alkalosis and hyperkalemia. The data failed to demonstrate, however, the appearance of the early transient hyperkalemia response which has been observed in humans in the early moments of hyperventilation. Blood pH rose from an initial level of 7.46 to 7.71 after 3-1/2 minutes of exposure to altitude. At 30 minutes, it had declined slightly from this maximal level to 7.63, suggesting the development of partial compensation to respiratory alkalosis. The results also indicate a temporal potassium-glucose relationship, potassium decreasing and glucose increasing simultaneously during exposure to altitude.

Goldfarb, B., and L. Lobian. The interrelationship of hypoxia, erythropoietin, and the renal juxtaglomerular cell. Proc. Soc. Biol. Med. 111(2):510-511 (1962). Others have noted the frequent association of increased juxtaglomerular (JG) of granularity and increased levels of plasma erythropoietin (EP) after the combined stimuli of underdistention of the renal arterial bed and hypoxia of the renal parenchyma. To separate these stimuli, rats were subjected to hypoxia without hypovolemia by being kept at 1/2-atmospheric pressure for 12 hours. There was no change in the JG granularity and, therefore, probably no change in their rate of secretion. However, EP levels were known to be high. This tends to disprove the hypothesis that the JG cells secrete EP.

Goldman, H. J., and M. R. Becklake. Respiratory function test: normal values at median altitudes and the prediction of normal results. Amer. Rev. Tuberc. 79(4):457-467 (Apr. 1959). Values for the subdivisions of lung volumes of subjects acclimatized at 5760 feet above sea level do not appear to differ significantly from sea-level values if account is taken of the differences in body size. On the contrary, the similarity of value reported from different laboratories is striking. In contrast, resting and exercise ventilation and maximal breathing capacity are significantly higher, and the resting arterial oxygen saturation is significantly lower at median altitudes. These results are in keeping with the findings of other workers. Formulas have been derived for predicting various subdivisions of lung volume from age and body characteristics, and it is justifiable to apply these formulas both at sea level and at altitudes, at least up to 5760 feet.

Gomez, G. E. Question of cardiac hypertrophy in residents of high altitudes. J. A. M. A. 137:1297-1301 (7 Aug. 1948). From the study of the transverse diameter of the heart by means of teleroentgenograms taken of 480 inhabitants of the city of Bogota (altitude 8016 feet) the following conclusions are reached: when the values of the transverse diameter are correlated with the height and weight of the patient, they are identical with the values obtained by Ungerleider and Clark for persons living at sea level. The constant,

$$\frac{\text{Weight X } 100,000}{\text{Height X (diameter)}^2} = 113.83,$$

determined by the same authors in pounds and inches, is found to be the same, when converted into kilograms and centimeters, as the constant for the 480 persons examined in Bogota. The formula in kilograms and centimeters is

$$\frac{\text{Weight X 100,000}}{\text{Height X (Diameter)}^2} = 2.47.$$

At 8016 feet above sea level, electrocardiographic signs of cardiac hypertrophy are not found as abnormal variations of blood pressure, pulse, number of respirations, respiratory capacity, or number of red blood cells.

Gömöri, P., and A. G. B. Kovach. The control of renal circulation in hypoxia. Acta Med. Acad. Sci. Hung. (Budapest) 16(1):43-60 (1960). In the dog with isolated cephalic circulation, arterial hypoxia, hypotension, and hypercapnia were studied for their effects on renal circulation. Normal conditions prevailed in the trunk during the experiments. Isolated cephalic (probably cerebral) hypoxia, hypotension, and hypercapnia were found to decrease urine flow, endogenous creatinine clearance, effective renal plasma flow, and the renal fraction of the cardiac output and to increase the renal vascular resistance. In some cases, it was possible to induce anuria

in all three states (from the head as its starting point). The changes in renal function proved to be reversible. Renal denervation or dibenamine treatment suppressed the effects of hypoxia. Adrenalectomy failed to inhibit the hypoxic effect on renal function. Nor did the denervation of the carotid sinuses exert any inhibitory action. It was concluded that renal vasoconstriction in hypoxia is mediated through the central nervous system.

Gömöri, P. Renal blood flow in arterial hypoxia. Acta. Med. Acad. Sci. Hung. 16(1):37-42 (1960). Arterial hypoxia induced by inhalation of a gas mixture poor in oxygen has been studied for its effects on the renal function of dogs anaesthetized with chloralose. It has been found to decrease the urine flow, the endogenous creatinine, the PAH clearances, and also the renal fraction of cardiac output, but to increase renal vascular resistance.

Gordon, A.S., F. J. Lornetta, S. A. D'Angelo, and H. A. Charipper. Effect of low atmospheric pressures on the activity of the thyroid reproductive system and anterior lobe of the pituitary in the rat. Endocrinology. 33:366 (1943).

Goria, A. The electrocardiogram in normal persons in conditions of acute hypoxia. Minerva Med. (Torino) 46(21):692-693 (Mar. 1955). Electrocardigraphy was performed in subjects rendered hypoxic near sea level (Torino) by rebreathing a mixture of 7.5-percent oxygen in nitrogen, and at high altitudes at Col d'Olen (3000 meters) and Plateau Rosa (3500 meters) by rebreathing environmental air. An increase of approximately 80 percent in cardiac frequency was noted in all subjects at sea level. ECG changes occurred primarily in the PT, TP, PQ, and ST intervals, and in the P wave. High altitude changes were found in the PT and TP intervals and in the T wave. In both hypoxic groups, an increase was found in the P wave by 20 to 50 percent, and a decrease in the T wave by 20 to 50 percent.

Goria, A., and L. Luria. The writing test in hypoxia in mountain climbers and normal subjects. Minerva Med. (Torino) 46(21):690-691 (Mar. 1955). The writing test was performed in alpine guides (16 to 24 years) and in normal subjects (24 to 30 years) rendered hypoxic by rebreathing environmental air in a closed circuit at high altitudes at Col d'Olen (3000 meters) or Plateau Rosa (3500 meters). Three periods were noted which corresponded to the degree of hypoxia: a latent period in which no disturbances in writing occurred; a phase

characterized by primary changes; and a critical phase manifested by a complete inability to write. Changes were observed first in the writing of numbers, especially of seven and eight. Some subjects displayed a degree of uncertainty in writing and required more time to perform the task. Alpinists did not have writing changes due to muscular rigidity, but normal subjects had complete contracture of the forearm which persisted for a while after the cessation of hypoxia.

Grandjean, E. Adaptation of human organism to mountain climate. Schweiz. Med. Wschr. 79:515-518 (11 June 1949).

Grandjean, E. Effect of sojurn in median altitude (1750 feet) on muscular tones, tactile sensitivity, patellar reflex, and blood formula. Helv. Physiol. Pharmacol. Acta. 7:277-290 (1949).

Grandjean, E. Variations of volume of hand in high mountain climate: plethysmographic study. Helv. Physiol. Pharmacol. Acta. 6:574-583 (1948).

Grandjean, E. Physiology of mountain climate. J. Physiol. (Paris) 40:51A-96A (1948).

Grandjean, E. The effect of altitude upon various nervous functions. Proc. Roy. Soc. (Biol). 143(910):12-13 (15 Dec. 1954).

Grandpierre, R. M. Disturbances of pulmonary ventilation at high altitude. Rev. Serv. San. Mil. 111:241-250 (Aug. 1939).

Grandpierre, R., C. Franck, and R. Lemaire. Reponses reflexes des centres respiratoires en fonction de la teneur en gaz respiratoires du sang au cours de differents etats d'apnee. J. Physiol. (Paris) 41:188 A-189 A (1949).

Grandpierre, R., and C. Franck. L'effet paradoxal de l'oxygene au cours des etats anoxemiques. Rev. Corps Sante Armees (Paris) 1:226 (1945).

Grandpierre, R., and C. Franck, Apnee provoquee au cours de l'anoxemie, par inhalation d'un melange gazenx riche en oxygene. C. R. Soc. Biol. (Paris) 138:255-256 (1944).

Grandpierre, R., C. Franck, and F. Violette. Effects of changes of the oxygen saturation of the arterial blood on the cerebrospinal fluid pressure. J. Aviation Med. 23(5):474-476 (1956). Changes of the cerebrospinal fluid pressure during progressive anoxemia were

studied in chloralized dogs. When anoxemia was induced by breathing of oxygen-deficient gas mixtures, the cerebrospinal fluid pressure increased gradually. When the anoxemic state was interrupted by inhalation of oxygen, the fluid pressure approached its normal level again; breathing air restored the normal pressure more slowly. If the anoxemia was not interrupted, the cerebrospinal fluid pressure continued to increase until respiratory arrest occurred; then it became stabilized for a short period, to decrease again (with decreasing arterial blood pressure) until the heart action stopped. After that, the decrease followed, more or less, that of the vencus pressure.

Gray, E. L. Appetite and acclimatization to high altitude. Milit. Med. 117(5):427-431 (Nov. 1955). A nutritional survey of troops in training at Camp Hale, Colorado (altitude range from 9,000 to 13,000 feet) revealed that the men did not consume enough calories to sustain body weight until acclimatization occurred. No evidence of anorexia was found and satiety was reached quickly. Caloric deficiency was largely carbohydrate in nature. The following concept is presented relating anoxia to body-weight loss: if anoxia is a limiting factor in brain metabolism and the level of carbohydrate within the central nervous system is the controlling appetite factor, then the satiety signal to the hypothalamus is prematurely set off and weight loss ensues.

Gray, G. W. Life at high altitudes. Sci. Amer. 193(6):58-68 (Dec. 1955). A description of the Institute of Andean Biology of the University of San Marcos, Peru, is based on a visit by the author to the institute and interviews with officials of the institute. The institute was established in 1928 to provide facilities for the study of the physiology of altitude adaptation and the effects of altitude on men adapted to sea level and to high altitudes. Observations by the research group of the phenomena of altitude adaptation are presented.

Graybiel, A., J. L. Patterson, and C. S. Houston. The changes in heart size in man during partial acclimatization to simulated high altitude. Circulation. 1(4[2]):991-999 (Apr. 1950). Previous studies have not led to a clear concept of the effects of anoxia on heart size. This paper summarizes pertinent literature and presents observations made on four healthy young men subjected to simulated high altitude in a decompression chamber over a period of one month. During the fourth week, the subjects were able to remain at 22,500 feet and on occasion were taken to higher altitudes for short periods. Size of the heart shadow, as revealed in teleroentgenograms, was determined at frequent intervals. The results are consistent in showing that the heart shadow decreases slightly in size while the subjects were exposed to reduced atmospheric pressures. Though slight, the decrease was too consistent to be explained by chance. Size changes tended only slightly to follow a pattern. It is concluded that during an early stage of acclimatization to severe anoxia under the conditions of this experiment, dilatation of the heart does not occur but rather the heart may decrease in size. Thus, reports that aviators develop cardiac enlargement after short exposures to high altitude are open to serious doubt. There is evidence that even in persons living for relatively long periods at high altitudes the heart does not change.

Greene, R. Acute anoxemia in the acclimatized person. Lancet. 2:683 (26 Sept. 1931).

Greene, R. Mental performance in chronic anoxia. Brit. Med. J. 5026:1028-1030 (4 May 1964). The mental effects of anoxia in mountain climbers are reviewed. Individuals are affected by anoxia very differently, some men showing little change within the limits of the experiments, and others being affected very much as they are by alcoholic intoxication. Memory and the capacity to perform mental work may be seriously affected. Emotional instability, usually in the form of irritability, may be severe. These emotional effects are observed in some cases after long stays at altitudes as low as 7,000 feet.

Greene, R. Composition of alveolar air on Everest, 1933. J. Physiol. 82:481-485 (12 Mar. 1934).

Grenell, R. G. Cerebral cortical potential in anoxia. Fed. Proc. 11(1):59 (1952). The effects of anoxia on the activity of cortical neurons were observed in cats breathing air, air mixtures containing 10- or 7-percent oxygen, or 100-percent nitrogen. Two types of responses to direct electrical stimulation were recorded: the "dendritic" and "neuronal" responses and the transcallosal response. The effects of anoxia on the components of these responses are under study with particular regard to the relative susceptibility of parts of the normal network to anoxia. Preliminary experiments with animals breathing 100-percent nitrogen showed that the transcallosal response was more markedly affected than the neuronal component of the ipsilateral response.

Grober. Altitude and circulation. Z. Ges. Phys. Therap. 35:10-23 (26 April 1928).

Grognot, P. Modification in the leukocyte count under the influence of decreased atmospheric pressure. C. R. Soc. Biol. (Paris) 146(15-16): 1241-1243 (1952). A group of 80 young and healthy subjects was exposed to a simulated altitude of 267 mm. Hg (equivalent of 8000 meters) for one hour. The number of lymphocytes decreased 20 to 40 percent, while the number of true leukocytes increased very slightly. In order to determine the threshold altitudes for the occurrence of lymphopenia, a number of subjects were exposed to a graduated series of decompressions. The threshold altitude was found to be between 5,000 and 5,500 meters, and the minimum duration to provoke a decrease in lymphocyte number at that altitude was found to be 35 to 40 minutes. Maximum values of lymphopenia were observed between 90 minutes and 2 hours after the conclusion of decompression and return to ground level. Return to normal leukocyte values was reached after four to five hours.

Grollman, A. Effect of high altitude on cardiac output and its related functions: an account of experiments conducted at the summit of Pike's Peak, Colorado. Amer. J. Physiol. 93:19 (1930). The effect of residence at high altitudes on the cardiac output and its related functions was investigated by comparing the results of measurements at sea level with those obtained on the summit of Pike's Peak. The cardiac output gradually increased on the summit of Pike's Peak, reaching a maximum of about 40 percent above its sea level value on the fifth day after arrival on the Peak. It then gradually declined again to its normal value. The relationship of this change to the hemoglobin content of the blood was demonstrated. The changes of the pulse rate, blood pressure, basal metabolism, alveolar gas tensions, and the effect of the ingestion of food on the cardiac output at high altitudes was also studied and the relation of these various factors to other physiological changes discussed. After a months' stay on Pike's Peak, a study of the cardiomuscular changes encountered on returning to a lower level was made.

Grossmann, M. Blood pressure at high altitudes. Z. Klin. Med. 102:86-101 (1925).

Grover, R. F., J. L. Reeves, D. H. Will, and S. G. Blount. Pulmonary vasoconstriction in steers at high altitude. J. Appl. Physiol. 18(3):567-574 (May 1963). Each of ten steers taken for 9 weeks to 12,700 feet (Mt. Evans, Colorado) showed a marked increase

in pulmonary artery (PA) pressure. These animals had PA pressures above 90 mm. Hg and one developed right-heart failure. The bovine species is remarkable for the severe pulmonary hypertension which develops during chronic hypoxia rather than for an excessive PA pressure response to acute hypoxia. The rate at which the pulmonary hypertension developed at 12,700 feet was extremely rapid compared to that at 10,000 feet. Therefore, not only the duration of the hypoxic stimulus but also its severity determines the response. The severity of the stimulus was augmented by the absence of a sustained increase in ventilation at high altitude. The pressure rise with acute hypoxia during the control period at low altitude and the dramatic fall in PA pressure when oxygen was administered at high altitude provided evidence for hypoxia-induced pulmonary vasoconstriction as an important mechanism in bovine pulmonary hypertension.

Grover, R. F., E. B. Grover, and J. K. Hagerman. Basal oxygen uptake of man at high altitude. J. Appl. Physiol. 18(5):909-912 (Sept. 1963). "When man native to low altitude is exposed to altitudes in excess of 10,000 feet, is there a change in his basal oxygen uptake?" This question was prompted by the unexpected observation of a 20-percent decrease in resting oxygen uptake of cattle and lambs at

high altitude. To elucidate this problem in man, multiple determinations of basal oxygen uptake were made on six individuals at both 5,200 and 14,150 feet. A small but significant increase in oxygen uptake was observed, probably reflecting the energy required to increase ventilation.

Guest, M. M. Diet and gastrointestinal symptoms at altitude. Fed. Proc. 7:46 (1948).

Gunderson, E. K., and P. D. Nelson. Adaptation of small group to extreme environments. Aerospace Med. 34(12):1111-1114 (Dec. 1963). In three studies at the Neuro-psychiatric Research Unit, subjective emotional responses, individual performance, and several aspects of a group functioning in extremely isolated Antarctic area were measured. Under conditions of restricted stimulation and activity for prolonged periods, participants reported an increase in the incidence and severity of emotional and somatic symptoms, particularly on items reflecting sleep disturbances, depression, irritability, and anxiety. The best single measure of effective individual performance was a standard score derived from peer and supervisor selections for group membership in a second expedition to the Antarctic. Three behavior areas contributed unique variance to the composite criterion. These areas, labeled emotional composure, social compatibility, and task motivation, were based on peer and supervisor ratings and yielded high multiple correlations (median R = 0.88) with the overall criterion for different station groups and for military and civilian personnel. Attitude measures revealed a general decline in work satisfaction, social relationships, and group accomplishment. Maintenance of group harmony and efficiency would appear to be a difficult but not impossible task in extremely isolated groups. Attitude measurements of group cooperation and achievement related consistently to an independent criterion of group effectiveness.

Gurdjian, E. S., W. E. Stone, and J. E. Webster. Cerebral metabolism in hypoxia. Arch. Neurol. Psychiat. 51:472-477 (1944).

Gursky, K. The effect of a sudden ascent to a mountain peak on the organism of a mountain climber. Teorie a Praxe. Telesne. Vychovy Sportu (Praha) 5(10):614-620 (1957). Physical examinations were carried out on young mountain climbers before and after a one-day, high-altitude tour. These included urinalysis, hematology, electrocardiogram, electrophoretic tests, and examination of physical functions. The data show a loss of gamma (3.4) and beta (2.15)

globulins and a 6-percent rise in albumin. The author interprets the changes as indicative of physical stress and the general adaptation syndrome. They may be considered as physiological peculiarities of an organism adapting itself to high altitude.

György, P. Acid-alkali balance at high altitude. Schweiz. Med. Wschr. 54:416-419 (1 May 1924).

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Hailman, H. F., M. Kessley, and E. Gellhorn. Influence of lowered barometric pressure on electroenephalogram. Proc. Soc. Exp. Biol. Med. 54:74-76 (1943).

Haldane, J. S. Acclimatization to high altitude. Brit. Med. J. 2:885-890 (15 Mar. 1924).

Haldane, J. S., A. M. Kellas, and E. L. Kennaway. Experiments on acclimatization to reduced atmospheric pressure. J. Physiol. 53:181-206 (1919).

Hale, H. B., K. I. Sydnor, and M. L. Sweat. Endocrine, cardiovascular respiratory and body temperature changes in man exposed to hypoxia combined with heat.' Fed. Proc. 13:65 (1954). To c ine the extent to which a moderately high environmental temperature may intensify or otherwise modify responses to mild hypoxia, nine different groups of young men were studied under standardized conditions in which the factors of oxygen pressure, environmental temperature, and time were varied.

Hale, H. B., and R. B. Mefferd, Jr. Metabolic responses to thermal stresses of altitude-acclimated rats. Amer. J. Physiol. 195(3): 739-743 (Dec. 1958). Exposure of fasting altitude-acclimated rats (390 mm. Hg, 18,000-feet simulated) for 24-hour periods to general level pressure (750 mm. Hg) at either cold (3°C), neutral (20°C), or hot (35°C) temperature seldom resulted in return of their metabolic functions to preacclimative "normalcy." Although the control and altitude-acclimated groups both were accustomed to neutral temperatures (24 and 26°C) quantitative differences at group level and altitude occurred in various indices of water, mineral and nitrogen metabolism. Of the 32 physiologic variables studied, only the rates of urine, volume of water intake, and urinary excretion of potassium, creatinine and glycine failed to differentiate the responses of the altitude- and ground-accustomed rats. The temperature response curves of the altitude group tended to parallel the corresponding ones for the control group, but most variables were on higher or lower planes. The difference in plane resulted either from the effects of the return to ground level pressure, or from non-reversible effects of acclimation to altitude per se.

Hale, H. B. Observations on men exposed to hypoxia at different environment temperatures. Fed. Proc. 12(10):59-60 (1963). Changes in circulatory, respiratory, body temperature, and adrenal cortical function were followed in male subjects during standardized exposures to low barometric pressure under two different conditions of temperature (80° and 120°F) in an effort to determine the extent to which adjustments to heat interfere with, or otherwise modify, the responses to hypoxia. In preliminary tests, the elevation in heart rate resulting from 15-minute exposure to an 18,000-foot simulated altitude was found to be slightly greater in 12 out of 19 subjects when they were in the overheated state. In the remaining 7 subjects, heart rates were elevated but not to the degree seen when the temperature was in the comfort range. The elevation in heart rate due to the heat factor was apparent both before and after the hypoxic phase, but a truly additive effect was not seen during hypoxia. Results from tests on a second group of subjects breathing a 10-percent oxygen-nitrogen mixture shows that time is an important element because there was a tendency for heart rates to decrease slightly after 15-minute exposure to hypoxia at 80°F, but at the higher temperature, heart rates either continued to climb throughout the exposure period or suddenly dropped to subnormal levels. In a comparative study now in progress, larger groups of subjects are being followed during exposures to a 14,000-foot simulated altitude with and without the heat factor.

Hale, H.B., G. Sayers, K.L. Sydnor, M.L. Sweat, and D.D. Van Fossen. Blood adrenocorticotrophic hormone and plasma corticosteroids in men exposed to adverse environmental conditions. J. Clin. Invest. 36:1642 (1957). Hypoxia (equivalent to that at 14,000-foot altitude), high environmental temperature (50°C) or hypoxia in combination with heat induced no detectable increase in the titer of ACTH in peripheral blood or in the concentration of plasma 17-hydroxycorticosterone, or corticosterone-like steroids of healthy male subjects exposed for brief periods (not in excess of 45 minutes). In a second experiment, three of five subjects who experienced hypoxia of this degree in a heated decompression chamber exhibited significant increases in the concentration of peripheral plasma 17-hydroxycorticosterone after 3 hours of exposure. In a third experiment, five of eight subjects exhibited increases in plasma concentration of corticosteroid after 2 hours of exposure.

Hale, H.B., and R.B. Mefferd. Effects of somatotropin on metabolic responses to cold, heat, and altitude. AF School of Aviation Med. 60-34:1-22 Randolph AFB, Texas (Jan. 1960). To study the actions of somatotropin (STH) on environmentally influenced metabolic activities and to test possibility that treatment with STH would be beneficial to mammalian organisms exposed to adverse conditions (cold, heat, or altitude), adult male rats were given low amounts of STH (0.5 mg. 100 gm. body weight) and exposed for 24 hours (fasting) to such conditions. Urinary nitrogen and electrolyte determination and certain ancillary determinations made it possible to appraise the metabolic states broadly in each case and to ascertain whether the administered STH modified metabolic responses to the different environments. STH prevented (either partially or completely) certain responses. But with low dosage, widespread metabolic control was not obtained. In particular, STH diminished or prevented the increases in urea and uric acid excretion and the urinary uric acid-creatinine ratio during acute exposure to heat (35°C), and the increases in creatine, uric acid-creatinine ratio, and the Na-K ratio during acute exposure to simulated altitude (18,000 feet). The administered STH had, in many respects, corrective effects or augmented (reinforced) adaptive changes during chronic exposure or during the initial phase of recovery from chronic exposures. Sensitivity to the injected STH varied with environments, with the length of time in an environment, and with the metabolic functions themselves.

Hale, H. B. Human cardioaccelerative responses to hypoxia in combination with heat. Aerospace Med. 276-287 (Apr. 1960). Insufficient work has been done to determine the time course of human cardiac responses to heat and hypoxia applied in sequence, nor does there seem to be published data on the variability in man with respect to reactions to hypoxia in combination with heat. The purpose of the present study was to fill this gap. Heat rate was used as the chief determination, and hypoxia equivalent to 14,000 or to 18,000-foot altitude was imposed either slightly later than heat or simultaneously with heat.

Hale, H. B., et al. Blood ACTH and plasma corticosteroids in man during exposure to simulated altitude and high ambient temperature. AF School of Aviation Med., AD 140 528, Randolph AFB, Texas. Hypoxia (equivalent to that at 14,000-foot altitude) acting alone, or in combination with high ambient temperature (50 ± 1°C humidity less than 20 percent) and high ambient temperature acting alone, induced no significant changes in the peripheral blood ACTH, plasma 17-hydroxycorticosterone, and corticosterone-like steroids of healthy male subjects exposed for periods of 15 to 45 minutes. In one experiment, 3 of 5 subjects who experienced hypoxia in a chamber heated to this same level exhibited an increase in the concentration of peripheral plasma 17-hydroxycorticosterone concentration at the end of 3 hours. In a second experiment, five of eight subjects exhibited an increase at the end of a 2-hour exposure.

Halhuber, M. J. Climatic and circulation on high mountains. Sportmedizin (Freiburg in Breisgau) 7(12):325-327 (Dec. 1956). The three phases of acclimatization to altitude are summarized. The first phase consists of a vagotomic reaction characterized by a slower pulse rate, decreased stroke and minute volume, and increased peripheral arterial resistance. Within a 1/2- to 1-hour period a shift to altitude amphotony occurs, manifested by an increase in pulse rate, enlarged minute volume, and decreased peripheral vascular resistance. At the same time, respiration deepens, CO_2 tension in the alveoli decreases, muscle tone increases, thresholds of sense organs are lowered, and the circulating blood volume and red-blood count are raised, due to the emptying of blood pools. The subjective symptoms are: excitability manifested by light finger tremor, hyperreactivity to sympathomimetics, and poor sleeping habits during the first days. The final phase may be described as an increased lability of the autonomic nervous system; it constitutes the endpoint of acclimatization to altitude. The author distinguishes further between "mountain sickness" and anoxia. Prophylaxis and therapy of mountain sickness have to be adjusted to the phase of acclimatization reached by the individual.

Halhuber, M. J., et al. Studies on the adjustment of the writer-sportsman to altitudes of 2000 to 3000 meters (6000 to 9000 feet). Med. Klin (Berlin) 53(7):256-260 (14 Feb. 1958).

Halhuber, M. J. Circulatory health and disease in high-mountainous climates. Munch. Med. Wschr. 101(26):1118-1123 (26 June 1959).

Hall, A. L., and H. R. Kelly. The effect of shouting on blood oxygen and alveolar carbon dioxide. Project NM 12 01 11 Subtask 3, Report No. 1, Naval School of Aviation Medicine Pensacola, Fla. (15 Nov 1957).
This is a report of an attempt to find word-per-exhalation combinations that would not decrease alveolar CO_2 tensions. The subjects repeated at certain intervals words whose articulation would result in maximal intrapulmonary pressure with minimal air flow. The results did not indicate a definite enough gain in CO_2 and O_2 to recommend this procedure in any emergency in which hypoxia and hypocapnia might be a contributing factor.

Hall, F.G. Regulation of breathing in man at altitude. Proc. Soc. Exper. Biol Med. 78:580-582 (1951). When man breathes ambient air at high altitudes, an hypoxic stimulus causes a rapid increase in pulmonary ventilation. The full effect of this hypoxic stimulus is counteracted, however, by concomitant hypocapnia. With the addition of carbon dioxide to inspired air, a more effective response to the hypoxic stimulus is manifested. It is concluded that while hypoxia and hypercapnia are separate stimulating factors and additive in their effects, the actual regulation of respiration at altitude depends upon the manner of their interaction.

Hall, F.G. Regulation of breathing of man at altitude. Fed. Proc. 11 (1[I]):63 (1952). Hypoxia and hypercapnia are separated but additive factors towards stimulation of pulmonary ventilation at high altitudes. The actual regulation of respiration at high altitude is, however, determined by the manner in which these two factors interact with each other.

Hall, F.G. Carbon dioxide and respiratory regulation at altitude. J. Appl. Physiol. 5:603-606 (Apr. 1953). Fourteen young men exposed to a simulated altitude of 22,000 feet breathed gas mixtures with varying concentrations of carbon dioxide. The partial pressures of oxygen and carbon dioxide in alveolar air were correlated with pulmonary ventilation measurements. The result indicated that hypoxic and carbon dioxide stimuli act independently to produce changes in pulmonary ventilation at altitude; when both are strong, they act additively. When, however the alveolar partial pressure of carbon dioxide falls below a certain level as a consequence of an increased alveolar ventilation, the level of that ventilation would seem to depend solely upon the strength of hypoxic stimuli.

Hall, F.G., D.B. Gill, and E.S. Guyman Barron. Comparative physiology in high altitude. J. Cell. Comp. Physiol. 8:301-313 (1936).

Hall, F.G., and J. Barker. Performance of acclimatized mice at altitude. Proc. Soc. Exp, Biol. Med. 86(1):165-167 (May 1954). Mice acclimatized to one altitude (350 mm.Hg) showed an increase in performance when exposed to a higher altitude (247 mm.Hg) as compared with ground-level control subjects. When acclimatized mice were bled, they showed a decrease in their performance level. This decrease in performance is not in proportion to the blood withdrawn, indicating that an increase in hemoglobin concentration is probably not the sole criterión for an increase in performance at altitude.

Haltgren, H.N., E. Marticorena, and H. Miller. Right ventricular hypertophy in animals at high altitude. J. Appl. Physiol. 18(5): 913-918 (1963). The weight of the ventricles and septum in formalin-fixed hearts were determined in six animal species living continuously at altitudes between 10,000 and 15,400 feet in the central Peruvian Andes. Control studies were made of a similar number of hearts obtained from sea-level animals. Guinea pigs, rabbits, dogs, lambs, pigs, and steers all exhibited a moderate hypertrophy of the right ventricle roughly equivalent to a 25-percent increase in weight. A lesser degree of septal hypertrophy occurred in all animals except steers. The data suggested that a moderate degree of pulmonary hypertension is the probable cause of the right ventricle hypertrophy. In steers, there would be roughly the equivalent of a mean pressure of 35 mm.Hg at 11,800 feet compared with sea-level pressure of 24 mm.Hg.

Hammonds, E.E. Myocardial infarction following reduction of atmospheric pressure in low-pressure chamber. Milit. Surg. 94:163 (1944). A case of myocardial infarction is presented. Because of a period of anoxia 12 hours before symptoms occurred, it is suggested that the anoxia was responsible for this infarction. There was a history of mild hypertension before the subject's exposure to high altitude and anoxia. Therefore, the best conclusion may be that all individuals having any evidence of cardiovascular abnormality should not be subjected to high altitudes, especially altitudes which produce more than 10-percent oxygen unsaturation of arterial blood.

Hansund, E., and H. Jungmann. Cardiovascular reaction in mountainous travel in the Alps. Med. Klin. Biol. 49 (19):775-777 (7 May 1954). Experiments were conducted to investigate the circulatory effects of changes in altitude. Twenty-eight healthy subjects were transported from altitudes of 2200 to 2300 meters daily for several days. Examinations were made at the start of the journey, at midpoint, and at the summit, and again on the return trip. Twenty-four subjects showed a decrease relative to the initial recordings in heart rate and minute blood volume upon arrival at the midpoint (1700 to 1900 meters) and an increase in corresponding vascular blood flow. Thus a vagotonic phase was indicated which lasted until the summit was reached. After 1/2 to 2 hours at the summit, this phase was replaced by a second amphotonic phase, indicated, in most cases, by an increased heart rate and stroke-and-minute volume. Several subjects showed an increased blood pressure without increase in heart rate, and some showed an increased heart rate without increased blood pressure. This phase reached a maximum, 1-1/2 to 2 hours after arrival at the summit and decreased after 3 hours. Upon descent, vagotonia was again noted, accompanied by fatigue. Similar experiments performed in a decompression chamber produced the second phase effect, but not the first. Of particular interest in the mountain experiment was the result obtained from a hyperthyroid subject, who showed no first but a strong second phase, and from two hypothyroid subjects, who showed a marked first but no second phase. One of the hypothyroid subjects, when given thyroid extract, eventually showed a small second phase. Further investigations of these effects would appear to be valuable in the study of circulatory disturbances.

Harboe, M. Lactic acid content in human venous blood during hypoxia at high altitude. Acta. Physiol. Scand. (Stockholm) 400(3):248-253 (1957). The concentration of lactic acid in human venous blood has been determined during hypoxia (subjects breathing atmospheric air at high altitude). Lactic acid concentration increases, depending on the degree and duration of hypoxia. Apart from heights of 15,000 to approximately 20,000 feet, where the lactic acid concentration increases simultaneously with increasing disability, such concentration is poorly correlated to functional disability during hypoxia.

Harnischfeger, E., and E. Optz. Cytochrome content of various organs of rabbits following adaptation to high altitude. Arch. Ges. Physiol. 252:627-635 (1950).

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Harris, E., and H. Jungmann. Altitude reaction of circulation in normal persons and in patients during sojourn in Alps. Schweig, Med. Wschr. 84:1265-1269 (6 Nov. 1954).

Harrison, T.R., C.P. Wilson, D.W. Neighbors, and C. Pilcher. The regulation of circulation: VII. The effect of anoxemia of mild degree on the cardiac output of unnarcotized dogs. Amer. J. Physiol. 83:275-301 (Dec. 1927).

Hartmann, H., and A. von Muralt. Effect of mountain climate on lactic acid in blood. Biochem. Z. 271:74-88 (1934)

Hartmann, H. Effect of adaptation on pulse and muscular power during oxygen deficiency. Luftfahrtmedizin 1:2-14 (1936).

Hartmann, H. Effect of adaptation to altitudes on pulse rate and muscular strength in oxygen deficiency. Luftfahrt-Med. Abhandl. 1:44-57 (1936).

Hartmann, H., and A. von Muralt. Pulse frequency and acclimatization. Acta Aerophysiol. 1(3):38-41 (1934).

Hartmann, H., and F. Moltenius. Physical efficiency and altitude tolerance in state of hunger. Luftfahrt-Med. 1:44-48 (1936).

Hartmann, H. Experimental observations of physiologic reactions (pulse frequency, muscular strength, and sensitivity at high altitudes) of members of German Himalayan Expedition, 1931. Z. Biol. 93:391-404 (1933).

Hartmann, H. Effect on human organism before and after adaptation. Verh. Deutsch Ges. Inn. Med. (Konig) 47:48-54 (1935).

Hartmann, H. Blood picture in high altitudes: experiments on members of German Himalayan Expedition, 1931. Klin. Wschr. 12:458-460 (25 Mar. 1933).

Hauty, G. T., R. B. Payne, and R. O. Bauer. Effects of normal air and dextroamphetamine upon work decrement induced by oxygen impoverishment and fatigue. J. Pharmacol. Ges. Ther. 119(3):385-389 (Mar. 1957). Sixty-four airmen were trained for 50 minutes at a compensatory pursuit task involving simulated aircraft indicators and controls. Half of the subjects were given 5 mg. of d-amphetamine and then required to perform the task for 4 consecutive hours at ground level. For the first 2 hours of work, all the subjects were returned to the first (sic) mixture. In the control subjects (without medication), normal air completely arrested proficiency degradation induced by the combined effects of hypoxia and fatigue, and sustained proficiency at a constant level. In the d-amphetamine group, normal air did not produce further proficiency increment, but d-amphetamine postponed the decline in proficiency which otherwise, would have occurred during the breathing of 12-percent oxygen.

Heber, A.R. Some effects of altitude on the human body. Lancet 1:1148 (1921).

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Hediger, S. Heart and high altitude. Klin. Wschr. 4:2109-2111 (29 Oct. 1925).

Hediger, S. Physiology of high altitudes. Schweiz. Med. Wschr. Schweiz. 53:352-357 (Apr. 1923).

Heemstra, H. Pulmonary vascular resistance during hypoxia; fast and slow reaction. Acta Physiol. Pharmacol. Neerl. (Amsterdam) 4(2):298 (Aug. 1955).

Heilmeyer, L., K. Recknazel, and L. Albas. Hepatic function and constituents, total composition and metabolism of blood in high altitude. 90:573-595 (1933).

Heimsoth, G. Pulse frequency and duration of systole during altitude adaptation on Monte Rosa following physical exertion and in acute oxygen deficiency. Z. Kreislaufforsch 34:329-335 (15 May 1942).

Hellebrandt, F. A., E. Brogdon, and S. L. Hoopes. The effect of acute anoxemia on hunger, digestive contractions, and the secretions of hydrochloric acid in man. Amer. J. Physiol. 3:451-460 (July 1935). Acute anoxemia of the pre-coma type has relatively little inhibiting effect on the secretion of hydrochloric acid by the normal human stomach, hunger contractions, or digestive motility. The exercise suppression of gastric function cannct be explained solely by an anoxemia hypothesis, and (when it occurs) is probably due to direct secretory and motor inhibition via the thoracic autonomics.

Hellems, H.R., F.W. Hayes, and L. Dexter. Pulmonary "capillary" pressure in man. J. Appl. Physiol. 2:24 (1949).

Hemingway, A., and G.G. Mahas. Effect of varying degrees of hypoxia on temperature regulation. Amer. J. Physiol. 170(2):426-433 (1952). Dogs were exposed to inhalation of mixtures containing 16-, 12-, 8-, or 6-percent oxygen, alternating with inhalations of normal air at a constant room temperature of 23°C. Rectal temperatures fell below normal during the hypoxic stages (from 38.25 to 37.65°C at 6-percent oxygen). When normal air breathing was resumed, the rectal temperature rose abruptly. The experiments revealed the following additional data: the oxygen consumption rate dropped sharply during the initial phase of hypoxic breathing, but rose again and after one hour exceeded the normal air values; and the respiratory quotient rose sharply during the first 8 minutes of hypoxic inhalation, then gradually dropped to pre-hypoxic values. It is concluded that mild degrees of hypoxia impair the physiological temperature regulation in a cold environment.

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Hensel, H., and G. Hildebrandt. Organ systems in adaptation: the nervous system. In Handbook of Physiology, (Adaptation to the environment) 4:55-72. In Dill, D.B., et al (ed.) Amer. Physiol. Soc. (1964). Data concerned primarily with slow adaptive responses, acclimation and, to some extent, phylogenetic adaptation, are reviewed. The following aspects involved in the regulatory and sensory adaptation to various environmental stimuli are included: general and theoretical aspects (adaptation and stabilization, the time factor, specificity of responses, and basic nervous mechanism) peripheral nerves and receptors (adaptation of nerve conditions, nerve functions in hibernators, and acclimatization and receptor activity), central nervous functions (habituation, cerebral cortex and habituation, changes in response patterns, shift in level of regulations, synchronization, behavioral adaptations, and neural control of endocrine responses); temperature adaptation in homeotherms (heat adaptations, cold adaptations in animals, and cold adaptations in man); adaptations to low oxygen tension (brain vascularization, anoxic tolerance of the brain, and changes in nervous functions); prolonged exposures to carbon dioxide, central nervous functions in hibernations (hibernation and hypothermia and arousal from hibernation); and adaptation in poikilo-organisms (capacity adaptations and resistance adaptations).

Henson, M., et al. Arterial oxygen saturation at altitude. Aviation Med. 18:149-157 (Apr. 1947). Results are presented on arterial oxygen saturation at altitude while subjects breathed air or oxygen. Associated findings are included on respiratory minute volume, respiratory rate, and pulse rate. On the basis of these, and of comparable data from the literature, revisions of the arterial oxygen saturation curves of the Handbook of Respiratory Data in Aviation are suggested.

Hepp, G. Medical observations during German Himalayan expedition, 1936: process of acclimatization. Munchin. Med. Wschr. 84:765-767 (May 1937).

Herbst, R. Reactions of circulation to diminution of air pressure. Verh. Deutsch, Ges. Inn. Med. 44:513-517 (1932).

Herlitza, A. Chemical equilibria of blood in mountain sickness. Arch. Fisiol. (supp) 24:676-691 (Dec. 1926).

Herran, M. Altitude sickness. Rev. San. Polic. (Lima)4:17-23 (Jan.-Feb. 1944).

Hershgold, E. J., and M. B. Riley. Diet induced variations in tolerance to altitude hypoxia in the mouse. Proc. Soc. Exper, Biol. Med. 100(4):831-834 (Apr. 1959). Mice on a diet containing large amounts of carbohydrate prior to exposure to altitude hypoxia survive at least five times longer than fasting animals, and significantly longer than animals on normal diet. When fasting mice were fed lipids of varying saturations, their tolerance was the same as that in the fasting state alone. Large amounts of fat added to the diet failed to decrease survival. Results demonstrate a solitary effect of carbohydrates on tolerance to hypoxia and show, as well, the inability of lipids alone to promote survival. Possible mechanisms for the protection provided by carbohydrates is discussed.

Herxheimer, H., R. Kost, and K. Ryjaczek. Gas exchange at high altitude during light and heavy work. Int. Z. Angew. Physiol. 7:308-325 (1933).

Herxheimer, H., E. Wissing, and E. Wolff. Muscular work and oxygen consumption at altitude. Z. Ges. Exp Med. 52:447-463 (1926).

Highman, B., and P. Altland. Effect of altitude and cobalt polycythemia, hypoxia, and cortisone on susceptibility of rats to endocarditis. Circ Res. 3(4):351-356 (July 1955). Rats with polycythemia, induced by exposures to simulated high altitudes, developed a significantly higher incidence of endocarditis following intravenous bacterial injections than rats with cobalt polycythemia of ground-level controls.

No increase occurred in altitude rats when polycythemia was prevented by repeated bleedings. These findings suggest that both polycythemia and hypoxia are necessary to explain increased susceptibility of altitude rats. Cortisone increased susceptibility of ground-level rats injected with Streptococcus faecalis. Unlike altitude exposures, however, cortisone did not render rats susceptible to endocarditis due to Hemophilus parainfluenza.

Hildebrandt, G., B. Ort, and H. Jungmann. Further investigations of adaptation to altitude in Obergurgl (2000 miles). Wien. Z. Inn. Med. 43(7):298-308 (July 1962). In a continuation of earlier investigations, this study undertook regular determinations of pulse rate, respiratory rate, blood pressure (in standing and prone positions), circulatory system analysis, and determinations of vital capacity as well as respiratory expiration strength. Records were made on 20 healthy students before and during 4 weeks in Obergurgl (2000 meters above sea level). In addition, the course of body weight and subjective well-being were monitored. The results confirm the hypothesis that acclimatization to this altitude is not due to a direct influence of the autonomic function, but rather consists of a phasic process which subsides only in the fourth week. It is possible to observe critical

periods for characteristics similar to those observed in cases of therapeutic rest at low altitude.

Hingston, R. W. G. Physiological changes at high altitude and their relation to mountain sickness. Indian J. Med 9:173-190 (July 1921).

Hirai, K., G. Atkins, and S. F. Marotta. 17-Hydroxycorticosteroid secretion during hypoxia in anesthetized dogs. Aerospace Med. 814-816 (Sept. 1963). Eight experiments were performed on five anesthetized dogs with adrenal vein cannulas. The secretion of 17-hydroxycorticostoroids markedly increased in animals breathing 10-percent oxygen for 2 hours at ground level. These animals showed a marked increase in heart and respiratory rates but not in adrenal vein blood flow.

Hittman, A. The treatment of anemia in high mountains. Wein. Med. Wschr. 106(9):208-211 (9 Mar. 1956). The physiological reaction of the organism to high-mountain climate can be roughly divided into general non-specific reaction up to a 3000-meter altitude, compensatory reactions (polyglobulin, etc.) up to 4500 - 5000-meter altitude, and decompensation above the 5000-meter altitude. The appearance of polyglobulin is a function of the altitude difference rather than of

the absolute altitude reached. It is characteristic of the immediate response (predominantly sympathetic) to rapid ascent in a decompression chamber. In contrast, rapid ascents to mountains on an elevator elicit a vagotonic reaction followed by altitude amphotonia with the sympathetic predominating. This second phase is similar to the period of altitude adaptation (7 to 8 days) characterized by polyglobulia, increased hemolysis and erythropoiesis, and hemoconcentration. Decrease of hemoglobin in presence of erythrocytosis is due to ultraviolet rays interfering with the incorporation of iron within the hemoglobin molecule. Mountain therapy of different anemias is discussed.

Hoagland, H., F. Elmadjian, and G. Pineus. Stressful psychomotor performance and adrenal cortical function as indicated by the lymphocyte response. J. Clin. Endocr. 6:301 (1946). Effects of mixtures of air low in oxygen on the efficiency of psychomotor performance have been determined in 1-hour runs on six normal persons and three psychotic patients operating the Hoagland-Werthessen pursuitmeter. The lymphocyte count falls with the stress of the experiments in normal persons and, in general, rises with the stress of the patients. In the normal group, the lower the drop in lymphocytes the greater the decline in efficiency of performance as measured by decline in the fatigue ratio ($r = -0.441$; $P < 0.01$). The patients show a rise in lymphocytes correlated with the fatigue ratio ($r = +0.381$) but this is not significant ($P \geq 0.05$). The difference in value between patients and controls is, however, statistically significant. In the normal group the stress is shown to increase the output of 17-ketosteroids as it lowers the lymphocyte count. The patients show anomalous changes in these variables.

Hoelscher, B. Mechanisms of altitude adaptation. The combined effects of hypoxia, adrenalectomy, and thymectomy in parabiotic rats. Endocrinology 54(2):147-153 (Feb. 1954). Three different types of parabiotic pairs of rats were established: Type I consists of intact (left) and intact (right) parabiotic pairs; Type II consists of intact (left) and adrenalectomized (right) parabiotic pairs; and Type III consists of thymectomized (left) and adrenalectomized (right) parabiotic pairs. Hemoglobin hematocrit, and red-blood cell count values were increased in both partners when hypoxia was imposed on one parabiont. Adrenalectomy of one parabiotic partner was followed by a compensatory hypertrophy of the adrenals left in the co-partner, which was higher in degree following exposure to hypoxia. There

was a marked difference in heart weight between the two partners when adrenalectomy was carried out in one partner (smaller in the adrenalectomized partner, more conspicuous when the nonadrenalectomized partner breathed an oxygen-deficient gas mixture). The livers of hypoxic partners when united with unexposed adrenalectomized partners showed a slightly fatty infiltration. Removal of the thymus had no appreciable effect. The adrenalectomized partner breathing ambient air in most instances died first when hypoxia was imposed on the co-partner. This suggests that the normal output of hypertrophied adrenal becomes critically insufficient for the adrenalectomized partner when the hypoxic partner has an increased demand for adrenal cortical steroids.

Hoff, E. C., R. G. Grenell, and J. F. Fulton. Histopathology of CNS after exposure to high altitudes, hypoglycemia and other conditions associated with central anoxia. Medicine. 24:161-217 (19 May 1945).

Hoffann, L. Mountain climate and athletics as cardiac stimulants. Wien Klin. Wschr. 50:1095-1098 (23 July 1937).

Hohwii, C. E., and W. H. Forbes. Study of circulation at rest and during exertion in high altitudes. Scand. J. Physiol. 76:75-87 (1937).

Hohwii, C. E. Oxygen consumption and respiratory function in high altitudes. Scand. J. Physiol. 76:88-100 (1937).

Holler, H., E. Schwarz, and M. Marti. The reaction of the adrenal cortex on ascent to high altitude. Acta Endocr. 16:118 (1954).
The gradual ascent to a high mountain area appears to be another non-specific stress reaction of the type credited to an increased secretion of adrenal-cortical hormone. Rail ascent to 8720 feet during 2-1/2 hours from Lauterbrunnen to Jungfraujoch, or to 5250 feet from Zurich to Davos, produced in eight healthy individuals a marked increase of circulatory thrombocytes and leukocytes, an increased excretion of 17-ketosteroids and of reducing costeroids, and a decrease of antithrombin titer; and, in six of the eight individuals, a 33.8-percent decrease of eosinophils. The results were not solely due to a decrease of partial oxygen pressure because an ascent in the low pressure chamber to a simulated altitude of 16,400 feet in 3-1/2 hours produced no change in thrombocytes and little significant change in the other determinations except that three of the six subjects manifested a 50-percent reduction in eosinophils. The authors believe that these findings are significant for bronchial asthmatics. Leisurely ascent to altitudes by the asthmatic corresponds in effect to an injection of ACTH.

Holmquist, A. G. Effect of high altitude and of mountain sickness on epinephrine, calcium and sugar content of blood, and its modification under influence of sun's rays. Acta Aerophysiol. 1:21-31 (1934).

Holmquist, A. G. Effect of various chemical substances on body temperature at sea level and in high altitude (3457 meters above sea level) Acta Aerophysiol. 1(3):16-28. (1934).

Honig, C. R., and S. M. Lenneg. Determinants of circulatory response to hypoxia and hypercapnia. Amer. Heart J. 53(5):687-698 (May 1957). Mechanisms responsible for circulatory changes in hypoxia and hypercapnia have been studied with an "aperiodic" ballistocardiograph. testerboard, and ancillary techniques. The results emphasize the necessity for measuring cardiac function in evaluating the effects of drugs or autonomic discharges for both the vasomotor center and chemoreceptors arterial ventricular contactibility as well as vasomotor tone. Circulatory performance in hypoxia and hypercapnia represents the resultant of cardiac depressant effects and opposing reflexly mediated alterations in contractibility and vascular tone.

Hornbein, T.F., and A. Roos. Effect of polycythemia on respiration. J. Appl. Physiol. 12(1):86-90 (1958).

Hornbein, T. F., Z. J. Griffo, and A. Roos. Quantitation of chemoreceptor activity. The interrelation of hypoxia and hypercapnia. J. Neurophysiol. 24(6):561-568 (1961). Carotid chemoreceptor activity was correlated with changes in arterial pO_2 and $[H^+]$ -pCO_2 in the artificially ventilated cat. A technique was used which afforded precise quantitative correlation of arterial blood gas tensions with electronically integrated chemoreceptor activity in Hering's nerve. Following sudden decrease of stimuli intensity, chemoreceptor activity reached a minimal level for several seconds and then rose slightly to a steady state. Chemoreceptor activity was present at arterial pO_2 of 100 mm. Hg and increased most as the oxygen tension was lowered from that value to 40 mm. Hg. A marked potentiation of the effects of hypoxia and increased $[H^+]$-pCO_2 upon chemoreceptor activity was demonstrated.

Hornbein, T. F. Evaluation of iron stores as limiting high-altitude polycythemia. J. Appl. Physiol. 17-243-245 (Mar. 1962). The total amount of iron available from normal body stores and usual dietary intake might be so small as to limit the rate and magnitude of the polycythemic response to high altitude. To evaluate this problem, the influence of iron supplementation on blood hemoglobin

concentrations was observed in ten members of the Himalayan expedition during the course of their ascent of a 25,660-foot peak. One-half of the group received iron supplements in large doses both orally and parenterally; the other five obtained only the iron present in the normal high-altitude diet. Hemoglobin concentration in both groups increased by 33 percent over a 2-month period. No significant difference in hemoglobin concentration between the two groups was noted at any time during the course of the study. It is concluded that normal iron stored plus dietary iron were adequate to meet the needs of increased hemoglobin synthesis at high altitude in the five individuals who received no iron supplementation.

Hornbein, T. F., and A. Roos. Effect of mild hypoxia on ventilation during exercise. J. Appl. Physiol. 17(2):239-242 (Mar. 1962). Hypoxia of mild degree (arterial oxygen tension above 60 mm.Hg) produces little or no ventilatory response in resting man during the steady state. To evaluate the possibility that the effectiveness of a hypoxic chemoreceptor drive might be enhanced by exercise, the ventilatory response to mild hypoxia was measured in two human beings during rest and exercise. Though no significant increase in ventilation occurred at rest above an arterial oxygen tension of

60 mm.Hg, a decrease in arterial oxygen tension from 100 to 94 mm. Hg produced a statistically significant increase in steady-state ventilation during moderate exercise. In addition, temporary block of the sympathetic innervation to the carotid and aortic bodies in one subject resulted in a diminution of work hyperpnea. This suggests that increased sympathetic tone during exercise, by reducing blood flow through the chemoreceptor, might result in increased neural discharge and, hence, increased ventilation even though arterial oxygen tension is the same as at rest. Thus, activity of the chemoreceptors was modified by sympathetic control of their blood supply, and may be an important determinant of the ventilatory response to exercise. Since work hyperpnea is enhanced by even mild hypoxia, this ventilatory response may be sufficient to initiate respiratory acclimatization to altitudes so low that resting ventilation on acute exposure is unaffected.

Hornbein, T. F., A. Roos, and Z. J. Griffo. Transient effect of sudden mild hypoxia on respiration. J. Appl. Physiol. 16:11-14 (1961).

Hornberger, W., and T. Benzinger. Disease due to reduction of atmospheric pressure. Luftfahrtmedizin 7:9-34 (1942).

Hortnagl, H. Behavior of pulse in persons climbing in high mountains of Bolivia for first time. Wien. Klin. Wschr. 43:774-778 (19 June 1930).

Houston, C. S. Acute pulmonary edema of high altitude. New Eng J. Med. 263:478 (1960). A case of acute pulmonary edema occurring in a healthy young athlete with a normal heart is presented. The condition is attributed to the combined stresses of cold, exertion, and anoxia occurring at 12,000 feet. Several other cases suggestive of a condition that may be termed "acute pulmonary edema of high altitude" are briefly reported. The mechanism of this condition is not known, but the disease, often fatal, deserves further attention by mountain climbers in particular.

Houston, C. S. The adaptations which produce acclimatization to oxygen lack. Aviation Med. 18:237-243 (June 1947). Oxygen lack, commonly though inaccurately known as anoxia, may result from several different physiological causes. In most instances, oxygen lack gives rise to respiratory and circulatory changes which tend to restore tissue oxygenation toward normal, and these changes are commonly known as acclimatization. A group of charts is presented to demonstrate that acclimatization to oxygen lack is the integration of a series of adaptations, one or more of which may be absent in any

particular case. The index of tissue oxygenation is taken as the mean capillary oxygen pressure, a theoretical value proposed by Barcroft which, together with tissue blood flow, determines the oxygen available to the tissues. Although the charts are principally used to analyze adaptation to high-altitude anoxia, they may be used with equal facility in the evaluation of adaptation to many other types of oxygen deficiency seen clinically. If the cha ts were drawn to larger scale on cross-sectional paper, many rapid theoretical analyses of accli natization could be made, using the mean capillary oxygen pressure as a measure of the success or failure of the adaptation.

Houston, C. S. Some observations on acclimatization to high altitude. New Eng. J. Med.. 253(22):964-268 (1 Dec. 1955). Man's only means of surviving exposure tc .ncreasing altitude is by an integrated series of adaptations, all of which tend to decrease the oxygen pressure difference between the environment air and the cells. Increased pulmonary ventilation raises alveolar oxygen pressure but lowers alveolar carbon dioxide pressure. To counteract the resultant respiratory alkalosis, base is excreted by the kidney, thus restoring the arterial pH to normal at a lower level of alkaline reserve. Cardiac output increases and also the oxygen-carrying power of the circulating blood which enables the delivery of more oxygen per unit of time to tissues. These changes allow heavy work by acclimatized men at altitudes that cause rapid loss of consciousness in unadapted subjects. Symptoms of oxygen lack and acapnia can be avoided in an unacclimatized subject by controlled voluntary hyperventilation. Personal experiences in mountain climbing and low pressure chamber ascents are included.

Houston, C. S., and R. L. Riley. Respiratory and circulatory changes during acclimatization to high altitude. Amer. J. Physiol. 149:565 (1947). Detailed studies of the respiratory and circulation changes which occur during the process of acclimatization to oxygen lack were made on four men exposed to gradually increasing simulated altitude during one month in a low pressure chamber. The data strengthen the concept that acclimatization consists of a series of integrated adaptations which tend to restore the oxygen pressure of the tissues toward normal sea-level values despite the lowered pO_2 of the atmosphere.

Houston, C. S. Operation Everest: Study of acclimatization to anoxia. USN Med. Bull. 46:1783-1792 (Dec. 1946). Despite excellent living conditions and adequate food and rest, the four subjects did not acclimatize to altitude either as completely or as rapidly as do mountaineers. The reason for this is not clear, but may be attributed to the confined quarters which made sustained and strenuous exertion impossible. At the higher altitudes, the men spent much of their time at rest, and this undoubtedly decreased their work ability just as is the case of a patient confined to bed. Evidence was obtained suggesting that the ability to tolerate high altitudes may depend on adaptation to the low arterial carbon dioxide pressure which results from hyperventilation and in turn raises the arterial oxygen pressure, content, and saturation. By lowering carbon dioxide pressure with hyperventilation acclimatized man is able to sustain arterial oxygenation at a higher level than can an unacclimatized man.

Hoyos, G. M. Normal values of circulatory and blood constants of inhabitants of Mexico, D. F. (2240 meters above sea level). Sem. Hop. (Paris) 27:3185-3191 (30 Oct. 1951).

Hudson, B. Some common mountain ailments and how to combat them. Lancet 2:1371-1372 (22 Dec. 1923).

Huff, R. L. Effects of changes in altitude on hematopoietic activity. Medicine 30(3):197-217 (Sept. 1951). The development of polycythemia (concomitant increase in red cells, hemoglobin, and red cell mass, proportional to the altitude of residence but without enlargement of the spleen or increase in white blood cells or platelet) is a major factor in the acclimatization to altitude. The purpose of the study was to investigate some of the aspects with the newer methods available; it was planned to determine the rate at which red cell production changes with variation in oxygen tension.

Hugin, F. Changes of pulse rate at median altitude. Schweiz. Med. Wschr. 86:907-909 (11 Aug. 1956).

Hügin, F., J. Keith, F. Verzar, and H. Wing. Changes in vegetative-autonomic excitability in high altitudes. Schweiz, Med. Wschr. 86(22):650-652 (2 June 1956). In 30 of 34 subjects, localized hyperemia after stimulation of the skin with anodized electrophoresis of 1-percent solution of pilocarpine was less pronounced and disappeared quicker at altitudes of 1800 meters (St. Moritz-Bad.) and of 3450 meters (Jungfraujoch) than at lower levels. This hyperemia was followed faster by a circulatory anemic reaction. These findings suggest either a decrease in the parasympathetic excitability of the

vasodilatators of the skin or an increase in excitability of the vasoconstrictor sympathetic axon reflexes of the skin, which constitute a reaction to the pilocarpine erythema.

Hultgren, H., and W. Spickhard. Medical experiences in Peru. Stanford Med. Bull. 18:76-95 (May 1960). In February and March of 1959, the authors spent a month in Peru examining research possibilities in the Peruvian Andes. A brief account of this trip may prove interesting framework for summarizing numerous scattered medical observations indicating areas for future medical research.

Hultgren, H. N., E. Marticorena, and H. Miller. Right ventricular hypertrophy in animals at high altitude. J. Appl. Physiol. 18(5): 913-918 (Sept. 1963). The weight of the ventricles and system in formalin-fixed hearts were determined in six animal species living continuously at altitudes between 10,000 and 15,400 feet in the central Peruvian Andes. Control studies were made of a similar number of hearts obtained from sea-level animals. Guinea pigs, rabbits, dogs, lambs, pigs, and steers all exhibited a moderate hypertrophy of the right ventricle roughly equivalent to a 25 percent increase in weight. A lesser degree of septal hypertrophy occurred in all animals except steers. The data suggest that a moderate degree of pulmonary hypertension is the probable cause of the right ventricular hypertrophy. In steers, this would be roughly the equivalent of a mean pressure of 35 mm.Hg at 11,800 feet, compared with sea-level pressures of 24 mm.Hg.

Hultgren, H., and J. Kelly. Pulmonary circulation in high altitude. Clin. Res. 9:104 (1961).

Hultgren, H., W. Spickard, and C. Lopez. Further studies on high-altitude pulmonary edema. Brit. Heart J. 24(1):95-102 (Jan. 1962). Six patients (five children and one adult) with acute high altitude pulmonary edema are described; they are residents of the Peruvian Andes. Either acute elevation of the left ventricular diastolic pressure or pulmonary venous constriction could be etiologic factors. The following factors may also be important in causing the syndrome: peripheral vasoconstriction and shift of blood volume to thorax due to anoxia, increase in blood volume, increased cardiac output due to anoxia, undue physical activity, myocardial anoxia, or increased capillary permeability due to infection or hypoxia. The attacks of pulmonary edema occurred from 9 to 36 hours after returning to an altitude of 12,250 feet from a stay at sea level varying from two days to two months. Two cases proved fatal.

Hultgren, H. N., W. B. Spickard, K. Hillriegel, and C. S. Houston. High-altitude pulmonary edema. Medicine 40(3):289-313 (Sept. 1961). Eighteen patients with acute pulmonary edema following exposure to an altitude of 12,200 to 15,300 feet were observed at the Chule General Hospital in La Oroya, Peru, from 1950 to 1959. The symptoms consisted of cough, hemoptysis, dyspnea, and weakness. Physical examination revealed tachycardia, cyanosis, and pulmonary rates. Bed rest and oxygen administration resulted in complete clinical recovery and clearing of the pulmonary exudate in 24 to 48 hours. Fifteen of the eighteen patients had been thoroughly acclimatized and developed pulmonary edema upon returning to the mountains after a one- to two-week stay at sea level. Although the most likely cause of the edema is acute left ventricular failure, x-ray studies revealed no evidence of left-ventricular or left-arterial enlargement. Pulmonary venous constriction, a shift of blood volume to the lungs, and a residual elevation of plasma volume from prior acclimatization are additional causative factors requiring investigation. Thirteen episodes of a similar syndrome occurring in mountaineers are described. Although such episodes have been previously considered

to be instances of pneumonia, their similarity to cases observed in Peru suggests that they also represent instances of high altitude pulmonary edema.

Hultgren, H. N. Pulmonary edema at high altitude: discussion in normal and abnormal pulmonary circulation. Presented at the Fifth Annual Conference on Research in Emphysema, Aspen, Colo., 13-16 June 1962.

Hunt, Sir J. The conquest of Everest, p. 276. New York, N.Y.; E. P. Dutton and Co., 1954.

Hurtado, A. Some clinical aspects of life at high altitude. Amer. Int. Med. 53(2):247-258 (Aug. 1960). A discussion of functional and organic changes in subjects acclimatized for long periods to high altitude is presented from observations made chiefly in the Peruvian Andes at an altitude of 14,900 feet. Alterations observed in healthy people living permanently at high altitude include electrocardiographic indications of right-ventricular hypertrophy and moderate pulmonary hypertension associated with low peripheral blood pressure, normal cardiac output, and increased lung blood volume. Of interest is the syndrome association with loss of tolerance to the low pressure environment, or "chronic mountain sickness". The varied symptoms indicating a loss of acclimatization include a considerable increase in circulative blood volume due to an elevated cell component, a decrease in plasma volume, erythropoietic hyperactivity, marked right heart hypertrophy, elevated cardiac output, accentuated pulmonary hypertension and low peripheral blood pressure, increased blood hypoxia, absence of the hyperventilation observed in normal acclimatized subjects, and decreased sensitivity of the respiratory center to CO_2 stimulation.

Hurtado, A., C. Merino, and E. Delgado. Influence of anoxemia on the hematopoietic activity. Arch. Int. Med. (Chicago) 75:284-323 (1945). Investigations have been made, at sea level and at high altitude, in several series of healthy and diseased male subjects, concerning the influence of temporary, intermittent and chronic anoxia (anoxemia) on the morphologic and other characteristics of the circulating blood. The related literature has been briefly reviewed.

Hurtado, A. Respiratory adaptation in the Indian natives of the Peruvian Andes: studies at high altitude. Amer. J. Phys. Anthrop. 17:137-165 (1932).

Hurtado, A. Studies of high-altitude blood observations on the Indian natives of the Peruvian Andes. Amer. J. Physiol. 100:487-505(1932).

Hurtado, A. Man in high-altitude habitats. An. Fac. Med. (Lima) 38(1):9-16 (1955). Compared to persons living at sea level (Lima, Peru, 500-foot altitude), persons living at high altitude (Morococha, Peru, 14,900 feet) demonstrated the following: reduced partial pressure of oxygen in the trachea, alveoli, and capillaries; shorter stature, lack of obesity, and greater thoracic breadth; hyperventilation phenomenon; polycythemia; increase in the total volume of circulating changes; and increase in heart size.

Hurtado, A., and H. Aste-Sulagon. Arterial blood gases and acid-base balance at sea level and at high altitude. J. Appl. Physiol. 1:304-325 (1948). The gas content oxygen saturation and the acid-base balance of the arterial blood have been determined in healthy residents at sea level and in Indian natives born and raised at high altitudes and living permanently at various levels on the Adean zone. Similar investigations have been made in different groups of newcomers at high altitudes within the first ten hours after arrival. The results obtained have been compared with those reported in previous and related studies.

Hurtado, A. Animals in high altitudes: resident man. In adaptation to environment, Chapter 54. Washington, D.C.: Amer. Physiol. Soc., 1964.

Hurtado, A., and R. T. Clark. Parameters of human adaptation to altitude. In Benson and Strughold (Ed.). Physics and medicine of the atmosphere and space, pp. 352-369. New York: John Wiley and Sons, 1960.

Hurtado, A. Some clinical aspects of life at high altitudes. Amer. Intern. Med. 53:247 (1960).

Hurtado, A. Mechanism of natural acclimatization. AF School of Aviation Med., Report No. 56-1, Randolph AFB, Texas (March 1956).

Hurtado, A. Chronic mountain sickness. J.A.M.A. 120:1278-1282 (19 Dec. 1942).

Hurtado, A. Acclimatization to high altitudes. In Cori, C. F., et al (ed.). Perspectives in Biology, pp. 348-352. Amsterdam: Elsevier Publishing Co., 1963. Various physiological aspects of man living in a high-altitude environment are presented. The adaptive mechanisms found in the high-altitude native fall, in general, in two

categories: mechanisms allowing a considerable economy in the drop of the oxygen tension gradient from the inspired air to capillary and mixed venous blood, and mechanisms concerned with an easier diffusion of oxygen from blood to tissues and its subsequent use by the active cells even in the presence of a low tension. Hyperventilation, circulating blood volume, pH level, tissue chemistry, diseases resulting from loss of acclimatization, pulmonary hypertension, and some cardiovascular processes are discussed.

Hurtado, A., et al. Mechanisms of natural acclimatization: studies on the native resident of Morococha, Peru, at an altitude of 14,900 feet. School of Aviation Med., AD102674, Randolph AFB, Texas (Mar. 1956). Investigation was made of the physiologic characteristics, at rest and during physical activity, in the Indian native resident of Morococha, Peru, a mining town located in the Andean region at an altitude of 14,900 feet (4540 meters) with an average barometric pressure of 446 mm. Hg. Comparative observations were carried out on healthy men living in Lima, (sea level). The native resident at high altitude, who lives with an alveolar oxygen tension of about 50 mm. Hg and an arterial oxygen saturation of 80 percent, exhibits definite adaptative mechanisms in the respiratory, hematic, and circulatory functions. The efficiency of these mechanisms is significantly evident in his behavior under the additional stress of physical activity, which is characterized, when compared to sea-level conditions, by a longer performance, a decreased energy cost, a lower production of lactic and pyruvic acids, and a reduced oxygen debt. These last characteristics suggest the presence of time adjustments which may constitute the fundamental basis of acclimatization to high altitudes.

Hurtado, A. Blood gas transport and acid-base balance at sea level and at high altitude. School of Aviation Med., Report 56-104, Randolph AFB, Texas (Oct. 1956). Investigations on the gas transport, the acid-base balance, and the electrolyte balance were carried out on the arterial blood of 80 healthy adult subjects living at sea level and in 40 native residents of Morococha, Peru, at an altitude of 4540 meters (14,900 feet). In a few subjects, mixed venous blood from the pulmonary artery was obtained simultaneously with the arterial blood, and similar measurements were carried out in both samples. From the aspects investigated, the data indicate that a permanent residence at high altitude presents definite and constant modifications in the circulatory blood.

Hurtado, A., and H. Aste-Salazar. Arterial blood gases and acid-base balance at sea level and at high altitudes. J. Appl. Physiol. 1:304 (1948). The gas content, oxygen saturation, and the acid-base balance of the arterial blood have been determined in healthy residents at sea level and in Indian natives born and raised at high altitudes and living permanently at various levels on the Andean zone. Similar investigations have been made in different groups of newcomers at high altitudes within the first two hours after arrival. The results obtained have been compared with those reported in previous and related studies. Observations show that the properties of the arterial blood under the influence of a low pressure environment are largely determined by the length of the exposure in addition to the level of pressure. A man just arrived at high altitudes differs from the temporary resident, and the latter, even if his residence is of a few weeks duration, does not reach the same characteristics observed in the man born and living permanently at high altitudes. The period of time which corresponds to the evolution of the process of acclimatization, and its merging into a condition of adaptation, is not known at present.

Hurtado, A. Chronic anoxia. Proc. Am. Scient. Cong. (1940) 6:169 (1942).

Hurtado, A. Aspectos fisiopatologicos y patologicos de la vida en la altural. Lima: Imprenta Editura Rimac S.A., 1937.

Hurtado, A. Gas content and oxygen saturation in arterial blood. Gac. Med. (Lima) 1:6 (Sept. 1944).

Hurtado, A., A. Rotta, C. Murina, and J. Pons. Studies of myohemoglobin at high altitude. Amer. J. Med. Sci. 194:708-713 (1937). Determination of muscle hemoglobin by Whipple's method have been made in dogs born and raised at high altitude, and its results compared with similar observations made at sea level. An increase of the hemoglobin content of the muscles has been found in the group of dogs at high altitude. It is suggested that this represents an important mechanism of adaptation to a condition of chronic anoxemia.

Hurtado, A. Pathological aspects of life at high altitudes. Milit. Med. 117(3):272-284 (Sept. 1955). A review is presented of studies on the natural acclimatization of native residents of Morococha, Peru, which has an altitude of 4540 meters (14,900 feet), and on the etiological role of anoxia in certain pathological conditions (pulmonary hypertension, chronic mountain sickness, polycythemia) observed at high altitudes. Included is a discussion on respiratory, circulatory, and physiopathological studies on normal residents and those with chronic mountain sickness.

Hurtado, A., N. Kaltreider, and W. S. McCann. Respiratory adaptation to anoxemia. Amer. J. Physiol. 109:626-637 (1934).

Husson, G., and A. B. Otis. Adaptive value of respiratory adjustments to shunt hypoxia and to altitude hypoxia. J. Clin. Invest. 36(2): 270-278 (Feb. 1957). Some bodily adjustments which may occur as a result of exposure to chronic hypoxia are studied. These adjustments are evaluated on the basis of their effectiveness in raising the oxygen tension of the body. Increased pulmonary ventilation is an important adaptation to altitude hypoxia. In chronic altitude hypoxia, the usual acid-base balance is one of compensated respiratory alkalosis. Adaptive adjustments to shunt hypoxia are also discussed.

Hustand, W. A., F. W. Stemler, and R. L. Jasper. Increased anoxic resistance resulting from short-period heat adaptation. Proc. Soc. Exp. Biol. Med. 88(1):94-95 (Jan. 1955). Mice exposed to heat in an

incubator at 36° to 37°C for 10 and 14 days were drowned in water of approximately body temperature. Heat adaptation was found to increase anoxia resistance to drowning (survival time) by 14.5 and 28.9 percent after 10 and 14 days, respectively. The effect is attributed to lowered basal oxygen requirements in heat-adapted animals.

I

Iakovlev, N. N., and L. G. Leshkevich. Effect of the nutritional factor on the acclimatization of competitive skiers to mountain conditions. Vop. Pitan. 19:9-15 (May-June 1960).

Imanaliev, M. I. Changes in arterial pressure, cardiac rhythm and respiration with normal and depressed functioning of the thyroid gland under mountain conditions. AFSC N65-17825, Foreign Technology Div., Wright-Patterson AFB, Ohio. The effects of the hypothyroid state on adaptation to hypoxia at 3200 meters altitude were studied on dogs with hypothyroidism induced by oral intake of 6-methylthiouracil (50 mg. per kg. body weight) for 11 to 12 days. At near sea level, blocking of thyroid gland function resulted in depression of blood pressure without significant changes in cardiac activity, slight increase in respiratory rate, and a decrease in amplitude of thoracic movements. In hypothyroid animals exposed to an altitude of 3200 meters, blood pressure was lowered, with a simultaneous increase in pulse and respiration rates. It is known that hypothyroidism depresses metabolism of the body. Therefore, animals with hypothyroidism could tolerate high altitude better than the normal control.

Ivanov, P. N. On the problem of the pathogenesis of high altitude emphysema. Pat. Fiziol. Eksp. Ter. 7:15-9 (Mar.-Apr. 1963).

Izquierdo, J. J. Maximum respiratory quotient in man at high altitudes: experimental apparatus formulae statistics. Gac. Med. Mex. 59:111-131 (Mar. 1928).

Izquierdo, J. J. Respiratory exchange in inhabitants of Mexico City. Rev. Mex. Biol. 7:101-106 (July-Aug. 1927).

J

Jackson, F., and H. Davies. The electrocardiogram of the mountaineer at high altitude. Brit. Heart J. 22(5):671-685 (May 1960). The electrocardiograms of twelve mountaineers were recorded at different altitudes up to 19,150 feet. Right-axis deviation and T-wave inversion in the right precardial leads were found in both European and Sherpa climbers, and S-T segments and T-wave changes in the left precardial leads in numbers of the European group. The significance of these changes is discussed.

Jackson, M. M., E. Shocket, and H. C. Dyme. The effect of moderate altitude upon human gastric emptying time. Aero. Med. Lab., Wright Air Development Center, Wright-Patterson AFB, Ohio, Tech. Report 52-74 (Mar. 1962). The relative difference in gastric emptying times was determined in volunteers at ground level or at simulated altitudes of 12,500 and 15,000 feet by serial roentgenography of the subjects' gastrointestinal tracts. A pressure-resistant x-ray-penetrable plastic window in the door of the decompression chamber permitted the x-ray films to be exposed without periodical removal of the subjects from the chamber. The films were taken five minutes, one hour, and two hours after eating, the results being tabulated according to the Annigers-Ing method (Gastroenterology, 8:711, 1947). The subjects were equilibrated at the simulated altitude for only 20 minutes before eating the standard Ba meal. The results indicated no significant difference in gastric emptying times at any of the test altitudes. An increase in altitude causes a decrease in oxygen and barometric pressure; these two factors are postulated to be mutually antagonistic in their effects on gastric motility, thereby multiplying the effects of each other and leaving the stomach to empty at a constant rate.

Jagic, N. Circulation at high altitude. Wien. Med. Wschr. 80:1223 (13 Sept. 1930).

Jalavisto, E., and J. Sundberg. The effect of exposure to low pressure, of restraining and of injections of adrenalin on the rate of reduction of methemoglobin in rabbit erythrocytes. Ann. Med. Exp. Fenn. 35(3):250-257 (1957).

Jaquet, A. Metabolic processes under reduced atmospheric pressure. Schweiz. Med. Wschr. 55:755-760 (13 Aug. 1925).

Jernigan, J. P., J. C. Cooley, W. L. Peterson, and G. E. Engle. Splenic infarcts associated with hypoxia. J. Aviation Med. 26(1):29-34 (Feb. 1955). Splenic infarction following high-altitude flight has been observed in eleven patients. The symptoms in all cases were initiated by pain in the upper abdomen within four hours after takeoff, and this was uniformly followed by nausea and vomiting. Examination routinely revealed left-upper quadrant and left-costovertebral angle tenderness. The peritoneal rebound phenomenon was frequently present within forty-eight hours. All patients had elevated white blood cell counts which increased with a rising temperature when the process progressively became worse. Positive tests for the sicklemia trait were obtained in seven cases. Roentgenographic studies frequently aided in the diagnosis by showing localized left-upper quadrant ileus, but splenic enlargement could not always be demonstrated. Although splenectomy is most frequently necessary in the treatment of such cases, it is believed that this decision can be made within forty-eight hour's observations.

Jezler, A., and A. Vischer. Morphologic blood changes after physical exertion in high mountains. Schweiz. Med. Wschr. 66:398-400 (25 Apr. 1936).

Johnson, L. F., J. R. Neville, and R. W. Bancroft. The effect of decreased barometric pressu. on oxygen consumption. Aerospace Med. 34:97-100 (Feb. 1963). The oxygen consumption of each subject at each barometric pressure considered is shown. The variations found from subject to subject at different altitudes are within the normal range of variations usually found at ground level. At 30 mm. Hg ambient pressure, five of the eight subjects showed a decrease in oxygen consumption from ground level values and two subjects showed an increase. While decreases in oxygen consumption outnumbered the increases, a statistical analysis of the variance between the means at different altitudes failed to show any significant differences which could be attributed to the decrease in barometric pressure. Variance ratio (F) was 0.58; F for 0.05 level of significance was 4.07.

Johnson, P. K. The effects of moderate altitude on exercise. Dessert. Abstr. 23(8):2965-2966 (1963).

Jongbloen, J. Effect of air on mental reactions; studies on reaction time at height of 5000 meters. Klin. Wschr. 14:1564-1568 (2 Nov. 1935).

Jong, D., H. Bruner, K. E. Klein, and H. M. Wegmann. The problem of cross adaptation in man. Presented at thirteenth General Assembly of the Advisory Groups on Aeronautic Research and Development, Athens, 10-12 July 1963 and the twentieth Meeting of the Aerospace Medical Panel, Athens, 5-10 July 1963. Pilots and astronauts have to dispose of an optimum resistance of their organisms in order to control extreme situations. The advantages of cross adaptation for human conditioning finds a partly discordant opinion in literature. Reported investigations were concerned with the physiological response of non-adapted persons, oxygen-want adapted subjects, and heat-adapted subjects in various standardized stressful situations. The course of some specific and non-specific adaptation processes and physiological reactions as well as the suppositions for positive cross adaptation in man are discussed.

Jungmann, H. Effects of mountain trips (Oberstdorf-Nebelhorn) in the cardiovascular system. Z · Ges. Exp. Med. 119(3):280-285 (1952). The physiological effects of relatively small altitude increases (1100 meters) were demonstrated on a group of 10 healthy subjects who undertook a trip by cable car from Oberstdorf, Germany (800 meters) to the nearby Nebelhorn mountain (1900 meters). All tests

were carried out two hours after arrival with the subjects at rest. An increase in pulse-wave velocity, attributed to a distention of the aorta and resulting in an increase of the cardiac output (in spite of decreased blood pressure), was observed. The pulse frequency increased while peripheral circulation resistance decreased. Deviations observed in five sympatheticotonic subjects are described.

Jurado-Garcia. A contribution to the study of acid-base equilibrium of the inhabitants of Mexico City. Bol. Med. Hosp. Infant. Mex. 20:663-676 (Sep.-Oct. 1963).

K

Kaiser, W. Reduction of oxygen in respiratory air. Med. Welt. 2: 1595-1599 (27 Oct. 1928).

Kaiser, W. High altitude effect on blood circulation. Med. Welt. 2: 973-975 (30 June 1928).

Kaiser, M. H., H. K. Ivy, L. Persner, J. P. Marbarger, and A. C. Ivy. Changes in bone marrow pressure during exposure to simulated altitude. Aviation Med. 22: 286-294, 311 (Aug. 1951). A method is presented for the measurement of bone marrow pressures. The bone marrow pressures of anesthetized dogs has a range from 12/8 to 117/96 mm. Hg with a mean of 52/41 mm. Hg. There was no change in systemic blood pressure with decompression. On decompression to simulated altitude of 40, 000 feet, while adequately oxygenated, the mean intramedallary pressure fell from 52/41 to 44/41 mm. Hg. There is a direct correlation between altitude and a fall in bone marrow pressure. This change in pulse pressure may be the result of either intravascular emboli or to a vasoconstriction of arteries of the bone marrow.

Kaiser, M.H., et al. Bone marrow and cutaneous circulation during decompression. AF School of Aviation Med. AD 52-666, Randolph AFB, Texas. (Aug. 195[illegible]) An investigation was made to determine bone marrow and cutaneous circulatory pressures in anesthetized dogs during decompression to simulated high altitudes (without hypoxia) and the influence of the sympathetic nerves on these changes. Normally, the bone marrow pressure varies from 12/8 to 117/96 mm. Hg with no correlation with the carotid arterial pressures. There was no change in systemic blood pressure with decompression, but there was a direct relation between decompression and the fall in bone-marrow pulse pressures. Unilateral sympathectomy resulted in a significant improvement of bone marrow pressures during decompression as well as significantly higher skin temperatures of the toes and forelegs when compared with the control legs. Decompression without hypoxia causes a fall in the skin temperature of the toes and forelegs. This fall in the skin temperature is presumably due, primarily, to an increased sympathetic tone of the cutaneous blood vessels, and may also be the result of the liberation of a small amount of adrenalin.

Kaminsky, P. Energy consumption and pulse rate during transportation of wood by sled in high mountains during winter. Arbeitsphysiol. 15:47-56 (1953).

Kasamatsu, A., and O. Creutzefeldt. Die latigkeit einzelner carticaler neurone und das elektrocardiogram der einer anoxic. Klin. Wschr. 166, (1956).

Katz, L. N., A. M. Katz, and F. L. Williams. Metabolic adjustments to alterations of cardiac work in hypoxemia. Amer. J. Physiol. 181 (3): 539-549 (June 1955). Metabolic changes during hypoxemia were studied in open-heart preparations (on dogs) in which circulation was relatively intact and the operation of nervous and humoral mechanisms was maintained. Correlations were seen in the relationship of both cardiac oxygen consumption and cardiac work efficiency, left cardiac output, and mean systemic arterial blood pressure. Cardiac efficiency was found to be independent of cardiac oxygen consumption, but increased when the arterial oxygen content was low. In individual experiments, exceptions to the correlation trends were noted; in several cases cardiac work increased with a fall in oxygen consumption or spontaneous changes in coronary flow occurred. The operation of mechanisms which are not dependent on circulatory hydrodynamics is, therefore, indicated.

Kaulbersy, J. Quantitative variations in potassium and calcium of red blood corpuscles under influence of high mountain climate. Bull. Internat. Acad. Polon. :481-494 (June-Dec. 1933).

Kaulbersy, J. Resistance of erythrocytes and number of reticulocytes. Z. Ges. Exp. Med. 86: 785-808 (1933).

Kellaway, C. H. The hyperglycemia of asphyxia and the part played therein by the suprarenals. J. Physiol. 53: 211-235 (1919).

Kellaway, C. H. Some physiological effects of anoxemia J. Physiol. 52:lxiii - lxiv (1919).

Kelley, V. C., and R. K. McDonald. Effects of acute exposure to simulated altitudes on dextrose tolerance and insulin tolerance. Amer. J. Physiol. 152; 250-256 (Feb. 1948).

Kellogg, R. H. Effect of altitude on respiratory regulation. Ann. NY. Acad. Sci. 109: 815-828 (June 1963). The alteration in chemical regulation of breathing, or, more specifically, the fall in B (zero ventilation intercept) as well as the rise in S (slope of the CO_2 response curve) occurring during acclimatization to altitude cannot be explained simply in terms of the blood acid-base changes, which are

not sufficient even to compensate for the respiratory alkalosis. It seems reasonable to suppose that there might be an adaptation to prolonged hypocapnia originally stimulated and maintained by the persistent hypoxic stimulation of the chemoreceptors. This suppositio would place the changes in altitude acclimatization at the opposite end of the same spectrum as the changes in chronic hypercapnia, as discussed by Schafer, but does not suggest the adaptive mechanism involved. One might speculate that the adequate stimulus produced by CO_2 inhalation may be effective pH in some region which is readily penetrated by CO_2 and less readily by other acids and which tends to change its acid-base characteristics, perhaps by active transport across its limiting membranes in such a way as to restore its own pH to normal within a few days (i.e. faster than the kidney restores the pH of the blood) despite continued depression of pCO_2.

Kellogg, R. H., N. Pace, E. Archibald, and B. Vaughan. Respiratory response to inspired CO_2 during acclimatization to an altitude of 12,470 feet. J. Appl. Physiol. 11(1): 65-71 (July 1957). The respiratory stimulation produced by adding graded amounts of CO_2 to the inspired gas was studied in four adult male subjects at sea level and during acclimatization to an altitude of 12,470 feet. During acclimatization, the curve relating respiratory minute volume to inspired or alveolar CO_2 shifted to the left by 8 to 11 mm. Hg, while the shape and slope of the curve did not change significantly, which indicates, primarily, a change in the magnitude of the response to a given level of CO_2. Most of the change occurred in the first two days at altitude. A possible mechanism is discussed which depends primarily on the initial hypoxic stimulation of the chemoreceptors. The mechanism might explain the shift in CO_2 response.

Kellogg, R. H., N. Pace, E. R. Archibald, and B. E. Vaughan. Respiratory responses to inspired CO_2 during acclimatization to altitude. Fed. Proc. 15 (1[1]): 108 (Mar. 1956). Four adult males were subjected to breathing various concentrations of carbon dioxide for successive ten-minute periods at Berkeley (sea level) and from three hours to eight days after arrival at Bancroft Laboratory (12,470 feet). During exposure to altitude, the curve relating respiratory minute volume to the inspired PCO_2 shifted markedly to the left, indicating a degree of 10 ± 3 mm. Hg in the PI_{CO_2} required for any given degree of respiratory stimulation. The simultaneous elevation and steepening of the curve was relatively slight. Thus, the change in carbon dioxide response appears to involve largely a change in "threshold" rather than sensitivity.

Kellogg, R. H., B. E. Vaughan, and D. W. Badger. Respiratory responses to acute changes in O_2 and CO_2 during acclimatization to high altitude. Fed. Proc. 16 (1[1]): 70-71 (Mar. 1957). Four adult male sea-level residents were studied at Berkeley (250 feet above sea level) and then flown to the White Mountain Research Station for additional study during residence of more than two weeks at the summit laboratory (14,250 feet.). "The alveolar carbon dioxide required to produce any given level of respiratory stimulation decreased about 13 mm. Hg during the first few days of acclimatization and, regardless of this large readjustment, was always about 1 to 3 mm. Hg lower when alveolar oxygen tension was fixed during the test below the hypoxic threshold (55 mm. Hg) than when... (sic) hypoxic threshold (100 or 225 mm. Hg)." These results indicate that chemoreceptor responsiveness to hypoxia remains essentially constant during respiratory acclimatization to this altitude, and not merely initiates the respiratory adjustments but also continues to contribute a small but significant stimulus to respiration throughout the large readjustments in carbon dioxide response.

Kellogg, R. H. The role of CO_2 in altitude acclimization. In Cunningham, D. J. C. and B. B. Lloyd (ed.). The regulation of human respiration, pp. 379-395 Oxford: Blackwell Scientific Publications (no date).

Kerwin, A. J. Heart size of natives living at high altitudes. Amer. Heart J. 28: 69-80 (July 1944). A study was made of the cardiac measurements as ascertained roentgenographically, of 273 normal native Peruvian male residents of high altitudes. The data obtained were compared with the normal predicted values for white persons living near sea level. As judged by the transverse diameter and frontal area, the size of the cardiac silhouette was definitely greater in high-altitude native residents than in normal white inhabitants of low altitudes. The average increases in transverse diameter and in frontal area was 11.5 and 16.3 percent respectively. In the age groups studied, no progressive enlargement with increasing age was evident. The possible mechanism and significance of this "enlargement" are discussed. It is suggested that this adaptive change may be one of a variety which occurs with prolonged exposures to low concentrations of oxygen.

Kessla. M. H. F. Haulman and E. Gellhorn. Studies on effect of anoxic anoxia on the central nervous system. Amer. J. Physiol. 140: 291-298 (1943).

Kestner, O., andH. Schadow. Sunlight, respiration and gaseous metabolism on the Jungfrau. <u>Arch. Ges. Physiol.</u> 217: 492-503 (1927).

Ketz, S.S., and C.F. Schmidt. Measurement of cerebral blood flow and cerebral oxygen consumption in man. Fed. Proc. 5: 264 (1946).

Keys, A. The physiology of life at high altitudes: The International Expedition to Chile, 1935. Sci. Monthly 43: 289-312 (1936).

Keys, A. Individual variations in ability to acclimatize to high altitude. Proc. Roy. Soc. (Biol.) 126: 1-29 (23 Sept. 1938).

Keys, A. Effects and processes of acclimatization Ergebn. Inn. Men. Kinderheilk 54: 585-671 (1938).

Keys, A., F.G. Hall, and E.S.G. Barron. Position of oxygen dissociation curve of human blood at high altitude. Amer. J. Physiol. 115: 292-307 (Apr. 1936).

Keys, A., J.P. Stapp, and A. Violante. Responses in size, output, and efficiency of the human heart to acute alterations in the composition of inspired air. Amer. J Physiol. 138: 763 (1943).

Khcmazyak, A.I., The reflex mechanism of periodic respiration in hypoxia. AFSC N65-1778, Foreign Technology Div., Wright-Patterson AFB, Ohio. Periodic breathing may be a result of the relative CO_2 and O_2 tensions in the circulating blood. Dogs, under

light anesthesia, inhaled a mixture of 10-percent oxygen and 90-percent nitrogen. The simultaneous values of the oxygen tension of blood in the carotid arteries, the arterial and venous blood pressure, and the pressure in the heart and the pulmonary arteries were also recorded. The experiments were repeated with periodic breathing induced by injections of sodium amytal solution. The ensuing hypoxia was registered by the lowering of oxygen tension in the carotid arteries, which led to an increase in respiration, pulse, cardiac stroke, and blood pressure of the systemic circulation. The systolic pressure in the carotid arteries was increased, but the diastolic pressure was lowered. Upon return to normal air inhalation, the first breath caused apnea, which was the result of the sudden increase in oxygen tension of the blood in the carotid arteries which, however, did not reach the normal level in the period of recovery from hypoxia. Periodic respiration ensued during the organism's normalization of the carotid chemoreceptors' threshold of sensitivity.

Kielik, A. M., and N. V. Sanotskaia. The significance of changes in pulmonary ventilation and circulation in the occurrence of hypoxic phenomena. Pat. Fiziol. Exp. Ter. 5(4): 30-34 (July-Aug. 1961). Comparative investigations conducted on healthy subjects, patients with cardiopulmonary insufficiency, and animals showed that

inadequate pulmonary aeration is responsible for the appearance of arterial hypoxia. This may be produced by a disturbance in the respiratory movements, e.g., breath holding, a disturbance in the relationship between inspiratory-expiratory activity, and an increase in the respiratory rate and non-uniform ventilation of different sections of the lung. A change from the vertical to the horizontal position reduces the blood oxygen saturation in healthy people by one-to-four-percent, due to non-uniform aeration of the lungs and a reduction of the pulmonary ventilation with simultaneous increase in minute volume. Oxygen breathing does not fully compensate for this phenomena.

Kindred, J.E. The effect of low barometric pressures on the structure of the kidneys of the white rat. Amer. J. Physiol. 3: 387 (Dec. 1943).

King, C.E., W.E. Garrey, and W.R. Bryan. The effect of carbon dioxide, hyperventilation and anoxemia on the knee jerk. Amer. J. Physiol. 2: 305 (Nov. 1932).

Kirchoff, H.W. Combined examinations of circulation and respiration under different oxygen concentrations. Rev. Med. Aero. (Paris) 2: 463-466 (Aug.-Sept., 1963). Respiratory oxygen concentrations of 14, 12, and 10 percent produced no change in oxygen consumption,

and only slight increases in carbon dioxide production, respiratory equivalent (ratio of respiratory rate to oxygen consumption), respiratory rate, and pulse frequency. Systolic blood pressure remained stable, diastolic pressure and heart rate were slightly decreased. Electrocardiographic studies showed no change in the ST segment or T wave. Ventilation with 8-percent oxygen resulted in a 30-to 50-percent increase in respiratory rate, an increase in pulse rate to over 100 per minute, and a significant increase in blood pressure. Subjects with respiratory difficulty reacted to mild levels of hypoxia with a marked increase in respiratory rate and respiratory equivalent. Pulse frequency was greatly increased in subjects with circulatory difficulty, and hypertensive subjects showed an increase in diastolic pressure. Subjects with cardiac-insufficiency showed significant changes in the electrocardiogram. It is concluded that tests of the effects of hypoxia on a variety of respiratory and circulatory parameters would be useful in the diagnosis of pathological conditions in pilots.

Klein, K. E., H. Bruener, and D. Jory. The importance of a long term sojourn in high mountain regions (Andes mountains) for the conditioning of flying personnel. Rev. Med. Aero. (Paris) 2: 110-211 (Dec 1961). It can be stated that the sojourn of several weeks at an altitude of 6,300 meters in a changing climate and performing moderate physical work, induces a marked adaptation in the unspecific hypophyseo-adrenocortical system, and, in addition, distinctly improves the reaction of circulation, respiration, metabolism, and other physiological functions to different stress situations. These results permit the conduction of an increased resistance against stressors, which are of importance with regard to flying performance and survival in emergency situations.

Klein, K. E., H. Bruner, and D. Jory. Influence of acclimatization to high altitude on the physiological response to stress. Industrial Med. Surg. 32 (2): 79-80 (Feb. 1963). The physiological responses of three persons participating in an expedition to the Andean mountains were examined prior to and a few weeks after their sojourn of four weeks at an altitude of 21,000 feet. A marked adaptation was found in the unspecific hypophyseo-adrenocortical system which improved the reaction of circulation, respiration, metabolism, and other physiological functions to different stress situations. The presence of corticosteroids enables the organism to produce the necessary protective reaction under stress. These results indicate that an increased resistance can be developed to the stressors that are of importance with regard to flying performance and survival in emergency situations.

Kline, R. F. Role of adrenal glands in the plasma and urinary electrolyte changes during moderate and severe anoxia. Fed. Proc 11 (1[I]): 84 (1952). Normal, nephrectomized, and splanchnectomized cats exposed to a simulated altitude of 28,000 feet for 90 minutes showed a decrease in plasma potassium. However adrenalectomized or nephrectomized-adrenalectomized animals showed no reduction in plasma potassium under identical conditions, which shows the predominant influence of the adrenal medulla at higher altitudes, causing large and rapid increases in plasma potassium value similar to those caused by injection of adrenaline.

Knoll, W. Athletic training in high altitudes. Deutsch. Med. Wschr. (Festschr d. Sportarztesch): 32-35 (1936).

Knoll, W. Blood at high altitude. Schweiz Med. Wschr. 54:121-127 (31 Jan. 1924).

Knoll, W. Problems of high mountain climate. Deutsch. Med. Wschr. 79: 819-820 (14 May 1954).

Kock, A. Working capacity of healthy individual during oxygen deficiency corresponding to altitude of 4000 to 8000 meters. Luftfahrtmedizin 3:214-215 (1937).

Kock, E. Circulation in high altitude. Luftfahrt Med. Abhandl. 1: 30-39 (1936).

Koepplin, F. Athletic medical problems and duties of medical officer in mountain regions. Schweiz. Med. Wschr. 73: 817 (26 June 1943).

Kolchinskava, A. Z., On the role of the age factor in adaptation of the human organism to oxygen insufficiency AFSC N65-17758, Foreign Technology Div., Wright-Patterson AFB, Ohio. Comparative studies of the response of human organism to the effects of atmospheric oxygen deficiency indicate that man between the ages of 20 and 50 possesses a more effective and economical adaptation mechanism to hypoxia than very young or very old individuals. With a decrease in ambient oxygen concentration, an increase in pulmonary ventilation and blood flow rate enable the organism to maintain homeostatis, and assures normal body functions. The adaptive mechanism may vary in each case. The increase in minute volume depends upon the degree of hypoxia, external temperature, individual characteristics, degree of training, and functional state of the nervous system.

Kolchinskava, A. Z. The effect of oxygen insufficiency on the higher nervous activity of man. Medychnyi Zhurnal (Kiev) 23 (2): 4-9. (1953). Rarefying the air in a pressure chamber to the equivalent of an altitude

of 5000 to 6000 meters or ascending Mount Elbrus to a height of 4250 meters produces a marked change in the higher nervous activity: the magnitude of conditioned reflexes is reduced, the latent period of response increases, the conditioned reflex is inhibited more easily by external agents, differentiation is arrested or delayed, conditioned inhibitions are disturbed, and phase and paradoxical reactions make their appearance. The above disturbances caused by reduction in barometric pressure are more pronounced at high mountain altitudes than in the pressure chamber. At actual mountain altitudes of 4250 meters, conditioned reflexes and, especially, differentiation reflexes develop with greater difficulty in non-acclimatized than in acclimatized individuals. As acclimatization proceeds, disturbances in the higher nervous activity begin to disappear.

Kollaritis, J. Hyperpyretic humidity, normal and hyperpyretic saturation deficit, and discharge of water from the lung at various body temperatures determined at several Swiss stations located at different altitudes. Schweiz Med. Wschr. 69: 252-254 (18 Mar. 1939).

Kollaritis, J. High altitude and the nervous system. Schweiz. Med. Wschr. 54:152-157 (7 Feb. 1924).

Koller, F., E. Schwarz, and N. Marti. Reaction of the adrenal cortex to ascent of high mountains. Acta Endocr. (Kabenhavn) 16(2):118-140 (June 1954). Two experimental series dealing with ascent to various altitudes were undertaken to determine the effect of altitude on the adrenal cortex. In the first series, 8 subjects ascended by rail from Lauberbrunnen to the Jungfranjoch (3450 meters). The following changes were registered: an increase in thrombocyte and total leukocyte counts, a decrease of eosinophils and anti-thrombin and an increased excretion of 17-ketosteroids and reducing corticoids. In the second series, carried out to test the effects of small differences in altitude, the same reactions were noted during ascent by rail from Zurich (450 meters) to Davos (1600 meters). It is concluded that "passive" ascent to high altitudes is accompanied by an increased secretion of adrenocorticol hormones. The alterations described may be explained as a non-specific stress reaction, the origin of which is not yet clearly understood. Experiments in a decompression chamber showed that a simulated altitude of 3500 meters was insufficient to evoke changes similar to those observed during ascent to the Jungfraujoch; however, a further simulated climb to 5000 meters showed a recognizable tendency to similar changes, although less pronounced. For this reason, it was concluded that a decrease of partial oxygen pressure is not alone responsible for the results obtained. Clinically, this reaction becomes important in cases of bronchial asthma, as the identical effect is obtained from passive ascent to high altitudes as from an ACTH injection.

Kolpakov, Ye. V., and N. M. Shumitskaya Influence of hypoxia under mountain conditions on dogs with Eck-Pavlov fistula. AFSC N65-17827, Foreign Technology Div., Wright-Patterson AFB, Ohio. The Eck-Pavlov fistula was selected as the model for reproduction of liver insufficiency. Behavior and peripheral blood-picture changes in dogs with liver insufficiency of long standing were compared with those experienced by dogs with Eck-Pavlov fistula, and with control animals to determine the nature and qualitative features of hypoxia adaptation. The postsurgical and control dogs showed differing response reactions under the conditions of hypoxia. The experimental animals suffered more severely than the control animals. In dogs with liver insufficiency, the mechanism of acclimatization to mountain climate went into action more slowly than that of the control animals. The investigations made on dogs with direct Eck-Pavlov fistula under conditions of hypoxia indicate significant participation of the liver in the hematogenetic processes and in the formation of hemoglobin.

Kopecky, M., and S. Daum. Adaptation of the myocardium to altitude anoxia. Cesk. Fysiol (Prague) 7 (3): 218-219 (May 1958).

Kornmüller, A. E., F. Palme, and H. Strughold. Electroencephalography as a method for studying altitude sickness. Klin. Wschr. 21: 5 (3 Jan. 1942).

Korner, P. I. Circulatory adaptation in hypoxia. Physiol. Rev. 39: 687 (1959). Because of the extensive investigation into the changes in cardiac output, heart rate, and blood pressure in arterial and tissue hypoxia, a fairly clear picture can be presented of the time course of the gross circulatory changes in these states. This article contains a bibliography of 400 references.

Korostovtseva, Nv. Effect of training on resistance of hypothermic rats to cerebral anemia. Biull. Eksp. Biol. Med. 56: 44-45 (Aug. 1963).

Korzhuyev, P. A., Physiological and biochemical mechanisms of adaptation to high mountain conditions. AFSC N65-17812, Foreign Technology Div., Wright-Patterson AFB, Ohio. Mountain sheep and goats showed higher hemoglobin and myoglobin concentrations and an increase in the erythrocyte number and the hematocrit, as compared with domesticated species.

Kosmolinskii, F. P. Effect of thiamine on tissue respiration in hypoxia. Vop. Pitan 15:73-75: Abstract in Int. Brit. Biol. Sci. 13:61 (1959).

Kosmolinski, F. P. Vitamin P as an effective substance for raising the endurance of the body to oxygen deficiency. Vop. Pitan 20:44-47 (Sep.-Oct. 1961)

Kovalenko, E. A. Oxygen tension in the brain of dogs at high altitudes while breathing oxygen. English translation in Sechenov Physiol. J., 47 (9): 1241-1250. New York: Pergamon Press, Feb. 1962. Brain oxygen tension was reduced in dogs by more than 1/2 of the cortex and 2/3 of the subcortex during an ascent without oxygen to a 12,000-meter altitude; pronounced hypoxic disturbances were noted at this time. When the dogs were raised to the same altitude while breathing oxygen, the oxygen tension was reduced by an average of 1/4 of the cortex, and 1/3 of the subcortex, without visible signs of hypoxic disturbances.

Kovalenko, E. A., V. L. Popkov, and I. N. Chernyakov. Polarographic method in study of tissue hypoxia in the living organism.

AFSC N65-17768, Foreign Technology Div., Wright-Patterson AFB, Ohio. A polarographic method for the study of tissue hypoxia in living organisms was utilized in dogs. As a cathode, a plexiglass electrode with a platinum needle was implanted into the brain tissue. An ebonite rectangular electrode with a silver chloride tip, or an ear clip with a silver chloride plate, served as an anode. This system permits a study of oxygen partial pressure in the brain tissue under conditions of low ambient pressure, acceleration stress, inhalation of pure oxygen under high tension or of various gas mixtures, and introduction of various pharmaceutical agents into the organism.

Kovalenko, E.A. A method for continuous registration of oxygen tension in the brain of dogs at low barometric pressure Pat. Fiziol. Eksp. Ter. 5:66-70 (Mar.-Apr. 1961).

Kovalenko, E.A. Oxygen tension in the brain of dogs in conditions of high altitude and during oxygen breathing. Fiziol Fh. SSR Sechendr. 47:1134-1141 (Sept. 1961).

Krasno, L.R., A.C. Ivy, A.J. Atkinson, and W.B. Johnson. Effect of exposure to anoxia of moderate degree on excretion of ascorbic acid in urine: preliminary report. War Med. 3:256-266 (Mar. 1943).

Kratochvil, C.H., S.S. Wilks, and W.A. Gerrard. Cigarette smoking at altitude. Abstract in Fed. Proc. 16(1^1):75 (Mar. 1957). Blood carbon monoxide was measured in a group of subjects before and after smoking one cigarette both at ground level and at 18,000 feet (altitude chamber). While the SAM complex coordinator was smoking cigarettes at ground level, at 18,000 feet and at 18,000 feet, his performance was measured. The results indicated that there was no increase in blood CO at altitude as compared with ground level controls after one cigarette. Similarly, there was only a slight decrement in performance when smoking while hypoxic at altitude when compared with the hypoxic controls. The primary physiological hazard in smoking at altitude appears to be hypoxia. Cigarette smoking causes little exaggeration of the effect of altitude hypoxia beyond that caused by the usual amount of carboxyhemoglobin formed.

Krestownikoff, N. Changes in leukocytes at altitude of 4200 meters. Arbeitsphysiol 6: 362-368 (1933).

Kreuzer, F., S.M. Tenney, J.C. Mithoefer, and J. Remmers. Alveolar-arterial oxygen gradient in Andean natives at high altitude. J. Appl. Physiol. 19:13-16 (Jan. 1964). The alveolar-arterial oxygen tension difference (A-aDO_2) was determined at three levels of oxygenation

in three groups of subject: normal persons at sea level, normal Andean natives at high altitudes, and Andean natives with chronic mountain sickness. The values of A-a DO_2 in the Andean natives were uniformly higher than in normal sea-level residents at all levels of oxygenation. These findings were accentuated in patients with chronic mountain sickness. It is concluded that there is no decrease in the diffusion barrier for oxygen, and there may be an increased veno-arterial shunting in the lung and wider distribution of ventilation-perfusion ratios in the high-altitude residents than in normal subjects at sea level; and part, at least, of the condition of chronic mountain sickness is an accentuation of these changes.

Kreuzer, F., et al. Alveolar-arterial oxygen gradient in the dog at altitude. J. Appl. Physiol. 15(5):796-800 (Sept. 1960). The effect of a sojourn of 5 days at an altitude of 14,300 feet (White Mountain, Calif.) on the alveolar-arterial oxygen gradient (A-aDO_2) in the anesthetized dog was studied at three levels of oxygenation. Two dogs breathed 11-percent O_2, air and 100 percent-O_2 at sea level, and air, 40- and 100-percent O_2 at altitude, with ventilization kept constant by means of a respiration pump. The alveolar samples were analyzed for O_2 and CO_2 pressures with the Scholander apparatus and the arterial O_2 pressures were measured in an

invitro polarograph. Control studies showed that the pump itself and hyperventilation had no effect on the A-aDO_2. The average values of A-aDO_2, 8.6, 23.4 and 168.5 mm. Hg at sea level (the three values refer to the respective three levels of oxygenation, the last figure corresponds to a shunt of about 12 percent of cardiac output) agreed well with previous data. The corresponding average values of A-aDO_2 at altitude were 3.3, 17.0 and 58.0 mm. Hg (corresponding to a shunt of about 4 percent). The A-aDO_2 breathing air was lower at altitude than when breathing an equivalent oxygen tension at sea level. The most dramatic effect consisted in a threefold decrease of the A-aDO_2 with 100 percent at altitude, indicating a decrease in true veno-arterial shunt flow.

Krogh, A. The anatomy and physiology of the capillaries. New Haven, Conn.: Yale University Press, 1929. The author mentions that he observed capillary dilatation during hypoxia.

Krupski, A, and F. Almasy. Physiology of blood in high altitude: study of morphology, chemistry and physical properties. Helv. Med. Acta 4:94-128 (Feb. 1937).

Kryszewski, A., and A. Szafranek. Effect of hypoxic-hypercapnic hypothermia on erythrocyte counts in rats. Acta Physiol Pol. 8(3-3a): 405(1957).

Kubicek, W.G. A study of the effects of hypoxia upon the course of fever in dogs and monkeys. AF School of Aviation Med., AD 80 074, Randolph AFB, Texas (May 1955). Experiments upon dogs and monkeys revealed that hypoxia may aggravate fever, especially during circulatory dysfunction. Reduced blood sugar and elevated plasma creatinine indicated the possibility of serious metabolic impairment during hyperpyrexia. Reduced blood carbon dioxide content with a small rise in pH was a usual finding. Blood oxygen content increased with increases in hematocrit. Histological studies showed tissue damage in the visceral organs by fever and hypoxia. Microscopic brain tissue studies on formalin-perfused animals failed to show conclusive histological changes in spite of severe neurological disturbances during the course of some of the experiments. The rapidity of the body temperature response to the onset of hypoxia may be of importance in flying at supersonic speeds and reaching altitude very rapidly. Under these conditions, the crew could be subjected to a sudden rise in environmental temperature and simultaneously a rapid decline in oxygen tension in the inspired gases.

Kulik, A. M. Neurohumoral shifts in the blood of animals under mountain conditions. AFSC N65-17824, Foreign Technology Div., Wright-Patterson AFB, Ohio. Neurohumoral changes were studied in dogs and domestic fowl under conditions of high altitudes. The inotropic and cholinesterase activity of the blood serum increased at 2000 meters. However at higher altitudes, values began to return to normal.

Kulik, A. M. On the inter-relationship of electrical activity on inspiratory and expiratory muscles of man in hypoxia, hyperoxia, and hypercapnia. Inst. Normal. Patol. Figiol, Akad. Med. (Nauk, SSSR) 6:105-106 (1962). Action potential of inspiratory (intercostal) and expiratory (abdominal oblique) muscles of three healthy subjects in the supine position are obtained with a superficial electrode and recorded on an electromyograph. As the electrical activity of the respiratory muscles was not striking in people at rest, the subjects breathed against both inspiratory and expiratory resistance, which increased the activity of the inspiratory muscles during inspiration and of the expiratory muscles during expiration. It is concluded that the inspiratory and expiratory zones of the respiratory center enter into complicated reciprocal relationships.

Kyazen, L. M., On the potential adaptive-compensatory function of the organism in hypoxia. AFSC N65-17773 Foreign Technology Div., Wright-Patterson AFB, Ohio. Pilots of supersonic craft are under physical and emotional strain that affects their respiratory rate (often resulting in hypoxia), cardiac rate, and other physiological parameters. The strain leads to a decrease of the subject's performance capacity. A study of the neural and gladular systems of the intestinal tract indicates that a prophylactic approach is necessary to prevent exhaustion of the central nervous and humoral systems mechanisms. Normalization of the metabolic processes can be achieved by the use of an adequate diet supplemented by vitamins, such as thiamine, citrin, and ascorbic and para-aminobenzoic acids. In certain cases, the use of pharmaceutical agents is advisable.

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Lalli, G. Histochemical mechanisms in acclimatization to high altitude. Riv. Med. Aero. (Roma) 2(21): 119-136 Jan.-Mar. 1958).

Lalli, G., and E. Sulli. Changes in blood coagulation in the course of acclimatization to high altitudes. Riv. Med. Aero. (Rome) 19(4): 606-618 (Oct.-Dec. 1956). Male rabbits exposed to a simulated altitude of 6000 meters for a period of 15 days showed a notable increase in platelet number; a decrease in coagulation and calcification times; a decrease in prothrombin time; but an increase in fibrinogen and total protein in the blood. During acclimatization to high altitude, the first phase of blood coagulation was notably accelerated. Clot retraction time was increased when the clot was free from adhesion, accompanied by an increase in hematocrit value; it was decreased when the clot adhered to the walls.

Lalli, G. Behavior of total lipids and some lipid fractions during acclimatization to high altitude. Riv. Med. Aero. (Rome) 20(1): 37-46 (Jan.-Mar. 1957). During acclimatization to a simulated altitude of 6500 meters, rabbits exhibited a phase characterized by lipemia. This phenomenon was caused by the increase of total, free, and combined beta-steroids, phosphatides, and, to a lesser degree, other lipid fractions considered as a whole, such as neutral fats, fatty acids, and steroids not precipitated by digitonin.

Lalli, G. Chemical tissue mechanism in acclimatization to high altitudes. Riv. Med. Aero. (Rome) 21(1): 119-136 (Jan.-Mar. 1958). This article is a review of research on biochemical mechanism of tissue during acclimatization to high altitude and covers the modifications of gaseous exchange during rest or work. Tissue respiration during anoxia is discussed in terms of enzyme-metabolite relationships in energy-transport systems. The role of myoglobin in acclimatization is discussed.

Lalli, G., E. Sulli, and G. Ghinozzi. Modifications in plasma and erythrocyte cholinesterases of the rat caused by acclimatization to high altitude. Riv. Med. Aero. (Rome) 18(2): 309-321 (Apr.-June 1955). Thirty rats exposed to a simulated altitude of 8000 meters for 12 days (following 12 days of acclimatization to lower altitudes) exhibited a total decrease of cholinesterase activity in erythrocytes by 28.69 percent and in plasma by 39.44 percent, as compared to control animals. No evident relationship was found between increase in the number of erythrocytes and plasma. This change cannot be attributed to possible variations of cholinesterase in young erythrocytes, the great number being formed under the action of the anoxic stimulus.

Lamb, L. E. Influence of aerospace flight on the normal cardiovascular system. Amer. J. Cardial.:8-18 (July 1960). Since the circulatory system is a transport mechanism, the work imposed on it must consider such pulmonary problems as a source of supply, the metabolic demands, and the hemotologic capability of the blood stream to carry oxygen. All these considerations, as well as the heart and blood vessels, must be considered in evaluating circulatory responses to the stresses of aerospace flight.

Lamb, L. E. Hypoxia - an anti-reconditioning factor for manned space flight. Aerospace Med. 36(2[1]): 97-100 (Feb. 1965). A problem area in manned spaceflight is deconditioning, caused by physical confinement and the decreased workload secondary to the absence of body weight. The syndrome of deconditioning results in a clinical picture of decreased biological activity manifested by numerous well-documented physiological adjustments. A large number of the physiological alterations noted in deconditioning are

exactly the opposite of those induced by hypoxia. A brief review is presented of the differences between the syndrome of deconditioning and the syndrome of acclimatization induced by prolonged hypoxia, thereby suggesting a means of counteracting at least a portion of the problems of deconditioning.

Lamb, L. E. Cardiac function and disease on acute and chronic exposure to altitude. G. P. 17(5): 88-93 (May 1958).

Lambertsen, C. T., H. Wendel, H. Chiodi, and S. Owen. Respiratory effects of 0.08 and 0.8 atmospheres of inspired pO_2, at a "constant" alveolar pCO_2 of 43 mm. Hg. Fed. Proc. $16(1^1)$: 76 (March 1957). Eight, 21, and 80 percent O_2 were administered at 1.0 atmosphere to 6 normal subjects maintained at an alveolar pCO_2 of 43 mm. Hg. In the absence of alterations in arterial pCO_2 or pH, 8 percent O_2 produced a 26-percent increase, and 80-percent O_2 produced a 15-percent increase in respiratory minute volume above the control values obtained during 21-percent O_2 breathing. The respiratory stimulation associated with 80-percent O_2 breathing was accompanied by a significant 1.6 mm. Hg rise in cerebral venous pCO_2, reflecting a central hypercapnia which may have produced the "oxygen" hypernea. Since neither cerebral circulation nor cerebral metabolism

was altered by 80-percent O_2, the internal jugular venous hypercapnia was due to diminished hemoglobin reduction. The hypoxic hyperventilation of 8-percent O_2 breathing was associated with a 5-mm. Hg fall in cerebral venous pCO_2, due to increased rate of brain blood flow. Therefore, it is possible that, despite a fixed arterial pCO_2, the chemoreflex respiratory response to hypoxia is, in part, counteracted by a fall in central stimulus level, brought about by hypoxic cerebral vasodilatation.

Langley, L. L., and R. W. Clarke. Reaction of adrenal cortex to low atmospheric pressure. Yale J. Biol. Med. 14: 529-546 (May 1942).

Langley, L. L., and C. H. Gunthorpe. Adrenal hypophyseal and pancreatic hormones in the liver glycogen response to low atmospheric pressure. Amer. J. Physiol. 191(2): 342-344 (Nov. 1957). The administration of 3 cc. of adrenocorticoid to rats at sea level fails to cause liver glycogen deposition. Under low atmospheric pressure, such animals accumulate about one percent liver glycogen. Adrenalectomyized-hypophysectomized rats maintained on a minimal dose of hypophyseal extract given 3 cc. of adrenocortical extract, and stressed, do not deposit liver glycogen. These results suggest that the hypophyseal hormones not only function to control the adrenal cortices under these conditions but also may contribute directly to the observed carbohydrate alterations. When larger doses of hypophysial hormones are used, there is a significant difference in liver glycogen between the stressed and nonstressed groups, indicating the possible repudiation of still another agent, perhaps insulin, since alloxan-diabetic rats do not accumulate liver glycogen in response to low atmospheric pressure.

Lapeyre, E. A. Form of respiration: contribution to physiology of Andeans. An. Fac. Med. (Peru) 26: 161-181 (1944).

Lapras, A. Tolerance to anoxia: Lessons of a Himalayan experience. Presse Med. 64(43): 1019-1021 (30 May 1956). Adaption of a technique of progressive acclimatization to hypoxia, in combination with usage of oxygen above 7000 meters, resulted in successful ascent above 8000 meters in the Himalayas with no illness or fatigue. Acclimatization was accomplished by the progressive establishment of camps at altitudes of 4700 meters for three weeks, 5,300 meters for two to three weeks, and at 6300 meters. At the end of the acclimatization period, resting climbers were able to remove their oxygen masks for several hours above 7000 meters with no difficulty.

Lapras, A. Aspects of respiratory pathology in relation to altitude. Presse Med. 66(63): 1420-1421 (17 Sept. 1958).

Laquer, F. Blood volume at high altitudes. Klin. Wschr. 3:7-10 (1 Jan. 1924).

Laquer, F. Effects of mountain climate on blood and exchange of fluids between blood and tissues. Klin. Wschr. 1:163-166 (21 Jan. 1922).

Larreta, J. A. Blood groups in natives of Andes Mountains. Rev. Med. (Peru) 12: 117-120 (April 1940).

Larreta, J. A. Serologic characteristics of native Peruvian children (up to 3 years of age) living in Andes. Cron. Med. (Lima) 58: 29-34 (Feb. 1941).

Lauer, N. V., A. Z. Kolchinskaya, and V. V. Turanov. On the adaptation of the mature organism to oxygen insufficiency and the importance of the higher divisions of the brain in this process. AFSC N65-17774, Foreign Technology Div., Wright-Patterson AFB, Ohio. A spirometer was used to study the effect of hypoxia in normal dogs in the low-pressure chamber employing various gas mixtures and under natural conditions of high altitude. The same effect was also investigated on anesthetized animals and in animals with cerebral decortication. In normal animals, moderate hypoxia resulted in an increase of the respiratory volume and respiratory rate. Severe hypoxia caused an increase in respiratory rate, a decrease in

alveolar ventilation, and an increase in heart rate. An ambient oxygen concentration drop to seven percent produced a sudden increase in blood pressure with a simultaneous decrease in cardiac rate. At this concentration, the oxygen saturation of the blood remained normal, but an increase in the red count was noted. Dogs under anesthesia, or with decortication, did not show the same degree of response. Thus, the conclusion may be drawn that a disturbance of the body function by the control of the nervous system, by the exclusion of cerebral cortex, decreased the reflex action which plays the basic role in the adaptive mechanism to hypoxia.

Lauer, N. V. On the role of the age factor in the organism's reaction to hypoxia. AFSC N65-17757, Foreign Technology Div., Wright-Patterson AFB, Ohio. Investigations showed that the mechanism of adaptability to oxygen deficiency in the ambient air was more effective in young adults than in immature or elderly persons. In youthful subjects, the reflexes of respiratory activity, the cardiovascular system, and the blood components are developed to full capacity, and the special hypoxia reflexes are well established. Also, the nervous and humoral systems are in a state of great stability. All these factors enable the organism to maintain a high degree of homeostasis.

Lawrence, J. H., _et al._ A physiological study in the Peruvian Andes. _Acta Med. Scand._ (Stockholm) 142(2): 117-131 (1952). The effects of high altitudes were investigated on three groups of test subjects: Group I consisted of 14 healthy medical students from Lima, Peru; Group II consisted of 11 normal natives from the region of Morococha (altitude 14, 900 feet); and Group III consisted of 4 native miners from Morococha suffering from high-altitude polycythemia and pulmonary silicosis. The following tests were carried out: blood volume determination (by the radioactive-phosphorus tagging method); plasma iron analysis; and determination of the plasma-iron turnover rate (rate of plasma concentration of Fe^{59} as a function of time). The following conclusions were drawn: the rise in red-cell count and hemocrit during the onset of high-altitude exposure can be attributed to hemoconcentration; tagging with Fe^{59} was found to be the most sensitive method for detecting changes in the rate of hematopoietic activity; altitude polycythemia differs from polycythemia vera in that the spleen fails to enlarge and thrombocytosis and leukocytosis are absent; there is no evidence of polycythemia vera among the natives acclimatized to high altitudes; and the fact that the iron turnover in the natives of Morococha decreased ten days after descent to sea level is remindful of similar changes in aplastic anemia.

Lawson, F. L. The effect of sulfanilamide on the ability of rabbits and dogs to withstand high altitudes. Amer. J. Physiol. 136:494-505 (1942).

LeBideau, G., and M. Berard. Work and nutrition at high altitudes; importance of glucides. Gaz. Med. France 65(19); 1517-1518 (10 Oct. 1958).

Legnani, F. Neuropsychiatric syndromes in relation to mountain climbing (tentative classification). Rassegna Guiliana di Medicina (Trieste) 11(5): 160-162 (May 1955). Included in a tentative classification of neuropsychiatric syndromes associated with mountain climbing are the following: syndromes caused by low atmospheric pressure (altitude sickness, characterized by a period of euphoria followed by mental depression); asthenic syndromes caused by fatigue due to muscular, nervous, and mental factors or fatigue derived from mental tension; syndromes caused by accidents (emotional and anxiety states, memory disorders); and instinctive syndromes with mental conflicts as related to mountain climbing (anxiety about reaching destination, self-preservation, and insecurity).

Lenggenhager, K. Studies on respiration and sickness at high altitudes and on respiratory regulation. Helvet, Med. Acta. 9:269-330 (April 1942).

Lenti, C., and M. A. Gullo. The effect of high mountains on phosphorolysis in skeletal and heart muscle. Naturweissenschaften (Berlin) 43(23): 541 (1956). Rats, maintained for 15 to 19 days at an altitude of 2961 meters, showed an increase of 32 percent in the phosphorylase activity of skeletal muscles over values observed in rats at 238 meters, and an increase of 26 percent in the activity of heart muscle. A suggested mechanism of the increase is the decrease in adenosine triphosphate known to occur during hypoxia.

Leubner, H. The effects of altitude climate and examination of suitability for mountaineering. Sportmedizin (Fierburg in Brusgan) 7(12): 329-335 (Dec. 1956). The results of experimental and field research on the physiological effects of mountain climate are reviewed in regard to its action on the autonomic nervous system (and, consequently, the circulatory regulation), stress effects on the pituitary-adrenal system, metabolic effects and organ changes. The author suggests certain diagnostic tests for examination of alpinists.

Leubner, H., F. Gabl, and I. Rabl. Ketosteroid excretion in bronchial asthma at high altitudes. Allerg. Asthma (Leipzig) 3(2): 79-82 (Apr. 1957).

Leulier, J. Basal metabolism and oxygen consumption on high mountains. Concours Med. (Paris) 76(52): 4865-4866 (25 Dec. 1954). Basal metabolic studies (oxygen consumption) performed in a mountain shelter at approximately 3000 meters show an average increase of 22 percent in two-thirds of the subjects, a decrease of 27 percent in the remaining third. After three minutes of the experiment, subjects with low basal metabolism fainted due to anoxemia. Fainting from the paradoxical effect of O_2, as observed in previous research, is compared with fainting observed in this experiment. The measurement of basal metabolism with effort showed an increase in O_2 consumption and no evidence of fainting. A transitory disorder of the endocrine regulatory centers, corti-corticothalamic centers, and anterior pituitary is also noted in subjects unable to adapt themselves to high altitudes.

Leusen, I., and G. Demeester. Effect of hypoxemia on the pulmonary circulation in the dog and cat. Acta Cardiol. (Brux.) 10(6): 556-575 (1955). In the cat, acute hypoxia induced by the inhalation or insufflation of a mixture containing 8-percent oxygen increased the pulmonary arterial pressure. In the dog, acute hypoxia induced by a mixture of 7- to 10-percent oxygen generally increased the cardiac output without augmenting the pulmonary resistance. The Stewart-Hamilton dye method was found to be more reliable than the Fick method for determining cardiac output in hypoxia.

Lewis, R. C., G. M. Kinsman, A. Iliff, and A. M. Duval. Effect of change of altitude on corpuscular constants. Amer. J. Clin. Path. 13: 208-214 (Apr. 1943). The corpuscular constants (mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and mean corpuscular volume) of Wintrobe have been calculated from the data obtained on the number of red cells, the hemoglobin content, and the packed red-cell volume of seven subjects, four of whom were studied at altitudes of 910, 5280, and 8720 feet above sea level, and the other three at the two lower altitudes. No definite trend in any of the constants occurs with an increase in altitude and all of the values are found within the ranges reported by Wintrobe.

Lewis, R. C., and R. Gorbin. Effects of graded hypoxemia on the pulmonary circulation of the dog. II: Moderate hypoxemia. Fed. Proc. 11: 93 (Mar. 1952).

Lewis, R. C., A. Iliff, A. M. Duval, and G. M. Kinsman. Effect of change of altitude on basal metabolism of human subject. J. Lab. Clin. Med. 28:851-859 (April 1943).

Lewis, R. C., A. Iliff, and A. M. Duval. Further consideration of effect on basal metaboiism: study on young women residents of Denver. J. Nutr. 26:175-185 (Aug. 1943). Ninety determinations of basal metabolism on forty-three young women residents of Denver between the ages of 17 and 26 years, inclusive, are reported. When the results of these determinations are compared with the values obtained in similar investigations at other altitudes during the last 15 years, the basal metabolism of the young women studied at Denver (altitude 5280 feet) is found to agree closely with, or to be lower than, the observations on women of comparable ages at elevations below 1000 feet. No consistent relationships exist between the basal metabolism of the young women observed in all of these studies and the altitudes at which the determinations were made. The relatively high values for basal metabolism at the higher elevation, reported in the literature cited as due to altitude, must be attributable to some other causative factor.

Lewis, R. C., A. Iliff, A. M. Duval, and G. M. Kinsman. Effect of change of altitude on blood of human subjects. J. Lab. Clin. Med. 28: 860-866 (April 1943). Determinations of the number of red cells, the hemoglobin content, the packed red cell volume, and the specific gravity were made on the blood of seven adult subjects (five women and two men) at Stillwater, Okla. (altitude, 910 feet) and at Denver, Colo. (altitude, 5280 feet). These same determinations were also made on the blood of one of the men and three of the women at Eldora, Colo. (altitude, 8270 feet). Although there was considerable variation in the amount of response of different individuals, and, in a number of cases, no significant change occurred, increases in the number of red cells, in the amount of hemoglobin, and in the packed red cell volume were found in the majority of instances with increases in altitude. Definite but insignificant increases in specific gravity were found to occur in the majority of the cases with each increase in altitude. With few exceptions, these changes in specific gravity were in the direction and of the approximate magnitude to be expected from the alterations in packed red cell volume.

Liebesny, P. Capillary circulation at high altitudes. Schweiz. Med. Wschr. 52:431-435 (4 May 1922).

Liebesny, P. Capillary circulation in high altitudes; comment on Lüscher's article. Schweiz. Med. Wschr. 53:777-778 (16 Aug. 1923).

Lilienthal, J. L. Effect of low concentrations of carboxyhemoglobin on "altitude tolerance" of man. Amer. J. Physiol. 145:359-364 (Jan. 1946). The effect of small amounts of COHb in man has been studied at altitude by means of measuring a sensitive visual function, the critical flicker fusion frequency (FFF), which is impaired by mild anoxia (9,000 to 12,000 foot altitude). Increments in COHb of the order of 5 to 10 percent resulted in appreciable deterioration of FFF at altitudes which alone did not affect the FFF (5000 and 6000 feet).

Lilienthal, J. L., R. L. Riley, and D. D. Proemmel. Arterial oxyhemoglobin saturation at critical pressure-altitudes breathing various mixtures of oxygen and nitrogen, with note on effect of exercise. Amer. J. Physiol. 145:427-431 (Jan. 1946).

Lilienthal, J. L., and R. L. Riley. An experimental analysis in man of the oxygen pressure gradients from alveolar air to arterial blood during rest and exercise at sea level and at altitude. Amer. J. Physiol. 147:199-215 (1946). By means of new techniques, measurements have been made in man of the oxygen pressure gradient existing

between the alveolar air and the peripheral arterial blood during rest and exercise at sea level and at simulated altitude. At rest, the gradient averaged 9 mm. Hg and during exercise 16.5 mm. Hg; the development of anoxia produced no significant changes in the size of the gradients. A method is presented for differentiating the total alveolar-arterial oxygen pressure gradient into its two main components, membrane resistance and venous admixture.

Lilienthal, J. L., and M. B. Pine. Effect of oxygen pressure on uptake of carbon monoxide by man, at sea level and at altitude. Amer. J. Physiol. 145:346-350 (Jan. 1946). The rate of uptake of CO has been studied in nine subjects at rest, under a variety of partial pressures of oxygen in the inspired air. The rate of uptake of CO may be predicted with considerable accuracy for sea-level and altitude conditions by means of the following relations of the "CO exposure index" to the increase in (COHb) = (pCO x time x minute respiratory volume) x 0.05. In accordance with the laws of combination of CO with Hb, in the presence of O_2, the rate of uptake of CO is inversely proportional to the partial pressure of O_2. Total barometric pressure plays no discernible role in the uptake of CO. Due to altitude, the effects of minimal anoxia sum with the effects of small amounts of circulating COHb to produce moderately severe symptoms of anoxia.

Lins, W. Lipase index and altitude. Rev. Med. Aero. (Rio) 7(1-4): 31-37 (Jan. -Dec. 1955). An increase in the blood lipase index was observed in 49 pilot-candidates and flight trainees exposed to a simulated altitude of 3400 meters in a decompression chamber. This indicates that atmospheric decompression causes lipase mobilization in the blood and lymphocytic lipase takes part, together with oxidase processes, in internal respiration.

Lipen, J. L., and W. V. Whitehorn. Role of changes in metabolism in acclimatization of albino rats to reduced barometric pressure. J. Aviation Med. 21:405-414 (1950).

Lippmann, A. Eyrthrocytes and blood volume in people living in high altitude. Klin. Wschrv. 5:1406 (30 July 1926)

Lisarraga, Moria L. Acute altitude sickness: acute pulmonary edema. An. Fac. Med. (Lima) 38(2): 244-274 (1955). A discussion is presented on the symptoms, pathogenesis, prognosis, and therapy of acute pulmonary edema caused by acute altitude sickness, along with its hematological x-ray and electrocardiographic aspects. Included are seven cases of disorders occurring in Peruvian natives living at high altitudes.

Loeschcke, H. H., U. Luft, and E. Opitz. Adaptation on Jungfraujoch: adaptation of respiration to altitude of 3500 meters and effect of ammonium chloride. Luftfahrtmedizin 7:218-227 (1942).

Loewy, A., and E. Wittkower. The pathology of high-altitude climate, p. 53. London: Oxford University Press, 1937.

Loewy, A. Biologic effects of mountain climate. Deutsch. Med. Wschr. 60:903 (15 June 1934): 60:9‿4 (22 June 1934): 60:990 (29 June 1934).

Loewy, A., and L. Pincussen. Changes in iron content of organs following irradiation and in high altitudes. Biochem. Z. 212:22-34 (1929).

Loewy, A. Action of high-mountain climate on morphology and chemistry of blood and its circulation. Klin. Wschr. 13:545-549 (14 April 1934).

Loewy, A. Protein metabolism at extremely high altitudes; limits of acclimatization. Inl. Z. Angew. Physiol. 3:596-604 (16 Dec. 1930).

Loewy, A. Acclimatization in high altitudes. Schweitz. Med. Wschr. 54:493-496 (29 May 1924).

Loewy, A. Effects of high altitude. Schweiz. Med. Wschr. 55:750-751 (13 Aug. 1925).

Loewy, A. Physiology of high altitudes with regard to pathology. J. State Med. 37:665-670 (Mar. 1929).

Loewy, A. New facts in regard to mountain sickness. Schweiz. Med. Wschr. 62:1173-1175 (17 Dec. 1932).

Loewy, A. Physiologic and Pathologic changes due to altitude. Rev. Med. Suisse Rom. 44:689-705 (Mar. 1924).

Loosen, H., and W. Heirnen. Cardiologic studies of mountain guides in Alpine sport centers with special regard to nervous heart. München Med. Wschr. 96:1372-1374 (19 Mar. 1954).

Lorentzen, F. V. Lactic acid in blood after various combinations of exercise and hypoxia. J. Appl. Physiol. 17(14):661-664 (July 1962). Seventy-five tests were made on military personnel ranging from 20 to 25 years of age. Exercise at a constant work load was done on a bicycle ergometer for 15 minutes at a chosen simulated attitude. The loads were from 400 to 1200 kg. —meters/minute and the simulated attitudes were from 10,000 to 17,000 feet. In these experiments

performed on a group of enlisted Air Force personnel randomly chosen, there was a very great deviation in results. This indicated that care must be taken in drawing conclusions about the conditions of stress and altitude from the amount of lactic acid present after an accident.

Lublin, A. Pathomorphosis of disease during life at high altitudes. Z. Klin. Med. (Berlin) 149(6)640-656 (1952). The pathological effects of high altitude are described, chiefly on the basis of personal observations made during a stay in La Paz, Bolivia (altitude, 3700 meters). Acclimatization to this altitude was found to be rapid if the arrival took place by aircraft rather than by railway (a 24-hour trip). An increase in erythrocyte number is almost immediate. While non-strenuous work does not cause as much discomfort as is generally assumed, any form of infectious disease leads to attacks of alternating dyspnea and polynea and other disturbances, and transfer to lower regions is indicated. Cardiac infarcts are frequent among non-natives, even at younger age. Arterial hypotension is common (blood pressure values of 82/45-70/50 mm. Hg were observed by the author). The high incidence of thromboangiitis obliterans (Buerger's disease) and of thrombophlebitis could be correlated with the altitude. Erythrocyte counts

carried out at La Paz revealed average values between 5.5 and 6.5 millions per cubic millimeter. It appears that humans suffer more from the effects of polyglobulism after return from higher to lower altitudes than vice versa. Cases of anemia are generally retarded or entirely stopped. Pernicious anemia is almost not found. Lymphocytosis values averaging 41 to 45 percent. The case of a pilot, in which attacks of gout were correlated with flights involving extreme attitude differences, is reported.

Luft, U., and E. Opitz. Adaptation on Jungfraujoch: increase in altitude tolerance during adaptation and after return to lowland. Luftfahrtmedizin 7:205-217 (1942).

Luft, U. Acute hypoxia and natural acclimatization. German Aviation Med. World War II, Dept. of Air Force, Washington, D. C. (1950).

Lundgren, N. P. V., E. H. Roosbach, and W. M. Boothby. Accuracy measurement of gaseous nitrogen elimination, using the closed circuit nitrogen meter method at altitude of 5000 and 14,000 feet. AD 25-670, Albuquerque. Nitrogen elimination was studied in the same subject at 5000 feet (at summit of Albuquerque, N. Mex.) and at altitude 14,200 feet (at summit of Mt. Evans, Colo.). Subjects breathed oxygen in the closed circuit recording gasometer system. Residual and tissue nitrogen was collected and then

analyzed with a Lilly-Anderson nitrogen meter. The nitrogen elimination of each subject was the same at both altitudes when the volumes were expressed at ambient pressure, body temperature, dry. Nitrogen elimination was proportional to the barometric pressure when the volumes were expressed at standard temperature and pressure, dry. The agreement of the results with gas laws indicates that the method could be employed by the Air Force in evaluating methods for the prevention of decompression sickness in aviators.

Lundin, G. Nitrogen elimination from the tissues during oxygen breathing and its relationship to the fat: muscle ratio and the localization of bends. J. Physiol. 152(1):167-175 (1960). The nitrogen content of end-tidal air during oxygen breathing was followed in human subjects and the nitrogen desaturation rate of the body was measured. The desaturation curve was separated into exponential fractions which were used to calculate the amount of fat and muscle tissue in the subjects. Blood flow through these tissues was also calculated. A relationship between nitrogen desaturation rate of fat tissue and decompression sickness appears to be probable.

Luria, L. The problem of nutrition while living on a high mountain. Ross. Clinicosci. (Milan) 32(11):294-296 (Nov. 1956). Subjects living at 100 to 1700 meters above sea level had a daily diet of about

3500 calories (with 1 liter of wine, 770 calories). The diet consisted of 435 calories of protein, 1850 glucides (52 percent), and 1170 lipids (37 percent). When these persons worked at high altitude on Mount Rosa (4560 meters), a daily diet of 5430 calories was used (with 770 calories for wine consumption), composed of glucides, 2300 calories (44 percent); proteins, 700 calories (13 percent); and lipids, 2250 calories (43 percent). All subjects maintained on this diet remained in good health and lost no appreciable amount of weight. Since loss of body water at high altitude is high, about two liters of beverages per day were permitted (tea, broth, and wine). At high altitude, a reduction in glucide values is noticed with a notable increase in protein and lipid values.

Luria, L. Acclimatization in high mountain and significance of pulse and pressure values in various body positions. Presented at V Congresso di Medicina Aeronautica, Napoli, 20-30 Sept. 1953. Parte III, Communicazioni, pp. 307-310. Pulse-rate measurements in persons living at an altitude of 4560 meters on Monta Rosa demonstrated variations in acclimatized subjects (25 to 40 years) in both horizontal and vertical positions; an increased rate in normal non-acclimatized subjects (21 to 61 years) in the vertical position; and a reduced rate in non-acclimatized subjects with altitude sickness

(20 to 51 years) in both vertical and horizontal positions. These findings may serve as an index of acclimatization. Arterial blood pressure in vertical and horizontal positions was not significantly altered in acclimatized and normal nonacclimatized persons. Systolic pressure was not altered in older subjects in the vertical position, but a 5- to 10-mm. Hg decrease was noted in the younger subjects.

Luria, L. Systematic investigations of the ortho-clinostatic cardiac reflex on the plain and in the mountains. Bol. Soc. Ital. Biol. Sper. (Napoli) 28(8-10):1662-1663 (1952). The heart rate was determined daily for 14 months in a 27-year-old healthy male subject adapted to the mountain climate. The tests were conducted on the plain and in the mountains at various altitudes. On the plain, the pulse rate in the standing position was 68 to 88 per minute (average 74); in the lying position, 52 to 78 per minute (average 62). In the test conducted at various altitudes, the following pulse rates (per minute) were obtained:

Altitude (meters)	Standing	At Rest (prone position)
1000 - 2000	70 - 88	60 - 78
2000 - 3000	74 - 88	72 - 88
3000 - 4000	80 - 96	76 - 84

Lurie, H. I. Normal hemotologic standards at altitude of 5740 feet (Witwatersrand, South Africa). Quart. J. Exp. Physiol. 33:91-105 (May 1945).

Lüscher, E. Capillary circulation in high altitudes: reply to Liebesny. Schweiz. Med. Wschr. 53:777-778 (16 Aug. 1923).

Lüscher, E. Blood circulation at altitude of 3460 meters. Schweiz. Med. Wschr. 53:509-516 (24 May 1923).

Lyman, R. S., W. A. Carlson, and O. O. Benson. Effects of reduced atmospheric pressures on electro-encephalogram. J. Aviation Med. 12:115-125 (1941).

Lyuban, G. L. The hormonal factor and adaptation to hypoxia in terminal conditions. AFSC N65-17803, Foreign Technology Div., Wright-Patterson AFB, Ohio. Hypoxia always appears as a component in terminal conditions, especially at the onset of clinical death. Injection of corticoids and antihistamines had a favorable influence on hypoxia adaptation in terminal conditions. It was found that adaptation to hypoxia is governed, primarily, by the hormonal effect of insulin. Experimental administration of hormonal preparations proved to have a marked positive influence on the dynamics of restoration of

vital functions. In experiments with white mice, resistance to hypoxia increased as the torrid stage of burn or electric shock became more severe. Adaptation to hypoxia is one of the components of the pathological process which occurs in terminal conditions of various types.

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Maag, C.H. Characteristics of mental impairment in hypoxia. Amer. J. Physiol. 70(2):243-247 (June 1957). An experiment was conducted to test the hypothesis that hypoxia produces an initial decline in mental efficiency, followed by a steady state which persists until the time of collapse. The steady state would be characterized by uniform performance interspersed with brief periods of inadequate performance which increase in frequency with the duration of stress, giving the appearance of a continuous decline in efficiency when performance is averaged over long intervals. The performance of ten subjects on a conceptual reasoning task involving classification was measured at altitudes of 13,000 to 18,000 feet to the point of collapse. Consideration of all data revealed a progressive decline in performance during hypoxia. When responses deviating by an arbitrarily determined value from individual subject performance were eliminated from the data, a constant level of performance was found for the later stages of hypoxia. The number of deviations in performance was also observed to increase with duration of exposure. The data obtained favors the concept of initial decline and intermittent impairment of performance in hypoxia, rather than a progressive decline.

Mackinnon, P. C. A study of various indices of adrenocortical activity during 23 days at high altitude. J. Endocr. 26:555-66 (Aug. 63). Measurements of urinary 17-hydroxycorticosteroids, 17-oxysteroids, pregnanediol, pregnenetriol, and circulating eosinophils were made at sea level and during a 23-day stay at high altitude. An attempt was also made to measure changes in emotional activity by means of the palmar sweat index (PSI). This index was assessed at intervals throughout the day at sea level and at high altitude, and in response to adrenocorticotropic hormone (ACTH) and a self-imposed stress. Within 24 hours of acute exposure to high altitude, urinary 17-hydroxycorticosteroids increased while circulating eosinophils decreased; by the fifth day both were returning to sea level values. The output of 17-oxysteroids was lower by the fifth day at high altitude and subsequently increased; pregnanediol and pregnenetriol levels remained unchanged. PSIs throughout the day became progressively lower as the length of stay at altitude increased. The response to ACTH at sea level and high altitude appeared to be similar but the response to a self-imposed stress was longer in duration at high altitude than at sea level.

Mackinnon, P. C., I. L. Mackinnon, and E. S. Williams. Effect of altitude on basal palmar sweating. Brit. Med. J. 5116:199-207 (24 Jan. 1959).

Maisano, A. Relation of weight and stature of natives to the altitude of Calabrian villages. Endocr. Sci. Cost. 26:66-74.

Mallison, K. Effect of altitude on gastric functions. Luftfahrtmedizin 4:156-165 (1940).

Malmejac, J., and A. Gross. Adrenal activity in anoxia: Connection between the nervous system, the medulla and the cortex of the adrenal gland. Med. Aero. (Paris) 7(4):451-454 (1952). Acute anoxia induces hyperactivity of both the adrenal medulla and the adrenal cortex. The mechanism involved is rather complex. Secretion of adrenaline by the medulla is under the direct influence of the sympathetic nervous system; the adrenaline liberated into the blood stream then stimulates the anterior lobe of the hypophysis, which in turn secretes a hormone inducing increased cortical activity.

Malmejac, J., and P. Plane. Influence of oxygen want on functional cortical fitness. J. Aviation Med. 23(2):177-180, 193 (1952). A conditioned salivary reflex was induced in dogs which had an external salivary

fistula (thus the reaction[illegible] sensory stimuli could be measured by the drops of saliva emerging from the fistula). The dogs were then subjected to anoxia either by breathing oxygen-deficient air or by altitude exposure in a decompression chamber. At exposure corresponding to an altitude of about 3000 meters (9800 feet), the conditioned salivary reflex was notably increased; at 5000 to 6000 meters (16,400 to 19,700 feet) the conditioned reflex (which is cortically controlled) decreased, while the innate reflex (subcortically controlled) was normal or even exaggerated; and at still higher altitude, both the innate and the conditioned reflexes were diminished. Frequent repetition of the tests with the same animal resulted in a certain degree of acclimatization, i.e., higher altitude had to be employed to elicit the same reactions.

Marbarger, J.P., S.A. Franzblan, G.F. Vawter, and R.W. Kecton. Altitude stresses in subjects with impaired cardicrespiratory functions: I. Control studies on normal subjects. School of Aviation Med., AD 95-149, Randolph AFB, Texas (Apr. 1952). Observations were made on the physiological response of 10 young healthy men who were subjected to simulated altitudes of 10,000 and 18,000 feet in a low pressure chamber while lying supine on a ballistocardiograph. The total effective peripheral vascular resistance was markedly decreased at simulated altitudes up to 18,000 feet. The response of the left ventricle was not significantly altered by a 10-minute exposure at 10,000 feet, but increased by about 50 percent after a 5-minute exposure at 18,000 feet. Administration of oxygen at the higher altitude caused an almost immediate return of both to ground-level values. Sudden exposure to ambient air at 18,000 feet increased both pulse rate and stroke volume, the former reaching a maximum in 10 minutes, but the latter continuing to increase with increasing exposure time. Increased stroke volume was responsible for the increase of cardiac output at high altitudes.

Marbarger, J.P., et al. Gaseous nitrogen elimination at ground level and simulated altitude and the occurrence of decompression sickness. School of Aviation Med., AD 95-149, Randolph AFB, Texas. Nitrogen elimination and amount of oxygen used were estimated during 2 hours of breathing oxygen in 33 subjects resting at ground level and at simulated altitudes of 8,000, 12,000, 18,000, and 22,000 feet. It amounted to 3598, 2580, 2148, 1774, and 1603 cc (standard temperature/pressure, dry) respectively. The incidence of bends at 38,000-foot simulated altitude after preoxygenation at these altitudes was compared to that without oxygen prebreathing. The results indicated that fewer descents were necessary after denitrogenation at ground level or any altitude than were necessary without denitrogenation. The data obtained confirmed the results of others in that at simulated altitude, less supplied oxygen was used with denitrogenation than at ground level.

Margaria, R., P. Cerretelli, and U. Bordoni. The regulation of pulmonary ventilation in acclimatization to altitude. Rev. Med. Aero. (Paris) 2: (Dec. 1961). It is evident from these experiments that the behavior of the acclimatized subject (as described in Figure 1(a) of the process of acclimatization) is assumed to consist of an acidosis induced by the urinary excretion of alkali, since this takes place during the hypoxic state. We may then expect that the behavior of the acclimatized man may be described by a curve made up by the first part of Figure 1(a), and which is shifted to higher values, ending somewhere in the middle with a curve which is the same as the second part of the curve in Figure 1(b).

Margaria, R., P. Cerretelli, and U. Bordoni. Regulation of pulmonary ventilation in acclimatization to altitude. Aerospace Med. 33:799-801 (July-Dec. 1962). The differential response to oxygen administration of the subject acclimatized to hypoxia appears to be associated with changes in the acid-base balance elicited by acclimatization. The decrease of the alkali reserve of the acclimatized subjects seems to be

responsible for the difference. This hypothesis is substantiated by the experimental finding that reduction of the alkali reserve, induced by NH_4Cl, produced in the acute hypoxic subject the same response to O_2 administration as in the acclimatized one. Hyperventilation of the acclimatized subject appears, therefore, to be sustained by the hypoxic stimulus. When the stimulus is removed, hyperventilation subsides and the hypoventilation which ensues involves a tendency to an acidotic condition which maintains a high level of ventilation.

Mark, R.E. Middle altitudes and hyperthyroidism. Arch. Exp. Path. Pharmakol. 116:334-366 (1926).

Marotta, S.F. Secretion of 17-hydroxycorticosteroids in conscious and anesthetized dogs exposed to simulated altitude. Proc. Soc. Exp. Biol. Med. 114:403-405 (Nov. 1963). Eighteen experiments were performed on eight conscious and anesthetized dogs in which the dorsal roots (T11-L3) had been severed and a glass cannula inserted in the lumbo-adrenal vein. Decompression to 17,000 feet simulated altitude for 2 hours while breathing ambient air (pO_2 78 mm Hg) caused marked elevation in 17-OHCS secretions in both conscious and anesthetized subjects.

Marpegan, H. S. Adaptation of young, healthy men to altitude (3450 meters above sea level). <u>Dia Med.</u> (supp.) 4:45-52 (19 June 1947).

Marshak, M. Ye. N65-17784 AFSC Foreign Technology Div., Wright-Patterson AFB, Ohio. When the oxygen content in the inspired air is lowered considerably, as in cases of hypoxia, the amount of oxygen used by the organism is smaller than its requirement, so that an oxygen deficiency develops and is aggravated as the hypoxia continues. By experimentation, it was shown that during the first few minutes after application of a tourniquet in the second phase of ischemia in the extremity, the muscle temperature dropped not only as a result of blood supply stoppage but also as a result of a conditioned reflex increase in the tone of the muscle and contraction of the vessels. Further, it was shown that after ligature of a branch of the coronary artery, the oxygen partial pressure drops very sharply in the ischemized zone of the myocardium. This suggests that oxygen therapy in myocardial infarct consists chiefly in elimination of the myocardial oxygen insufficiency in the zone bordering the zone of total ischemia.

Marticorena Pimentel, E. Probable effect of high altitude in the determination of the persistence of the ductus arteriosus: observations on

3000 school children at altitude. Rev. Med. Peruana (Lima) 26(323-324):421-430 (Nov.-Dec. 1955). Four cases of patent ductus arteriosus were found in Andean natives residing between 3000 and 3500 meters of altitude (0.47 percent of the population); three cases in persons between 4000 and 4500 meters (1.02 percent), and two cases at 4500 to 5000 meters (1.10 percent). All persons were between 12 and 16 years of age. The etiological role of high altitude for this abnormality is noted with reference to (1) anoxemia caused by low barometric pressure; (2) increase in pulmonary artery pressure; and (3) hypotension of the systemic circulation.

Mateeff, D. Gravitation disturbances of circulation under influence of decreased air pressure; study of mountain sickness. Acta. Aero-Physiol. 1(1):72-78 (1933).

Mateo, J. A. A. Role of vegetative nervous system in cardiovascular changes at high altitude. Rev. Clin. Esp. 4:112-116 (30 Jan. 1942).

Matsunobu, M., and K. Yogi. Composition of blood in mountain climate: polyglobulia in inhabitants at high altitude. Taiwan Igakkai Zasshi. 37:1133 (July 1938).

Matsunobu, M. Composition of blood in inhabitants of high mountain climates. Taiwan Igakkai Zasshi. 36:2174-2175 (Sept. 1937).

Matthes, M. Polyglobulia and altitude acclimatization. Deutsch. Arch. Klin. Med. 202(30): 377-384 (1955).

Matthes, M. Influence of polycythemia on altitude acclimatization. Jahrbuch der Wissenschaftlicher Gesellschaft für Laftfahrt (Braunschweig) pp. 194-200 (1955). Experiments were conducted to explore the role of polycythemia in altitude acclimatization. Six subjects ascended repeatedly to 7500 meters altitude in a decompression chamber without oxygen. Afterwards, they received transfusions of erythrocyte sediment, which raised their hemoglobin level by 15 to 20 percent, and the above series of ascents was repeated. The increase in tim. reserve and in ceiling values was very small and persisted when hemoglobin was reduced to normal by bloodletting. It is concluded that induced polycythemia does not improve altitude tolerance. An increase in the erythrocyte number evoked by altitude is effective only as a part of the total adaptive process.

Mathews, B. Limiting factors at high altitude. Proc. Roy. Soc. Biol. 143(910):1-4 (15 Dec. 1954). It is clear from oxygen failures in

flying, that exposures of less than an hour to altitudes above 15,000 feet may produce permanent brain damage in the unacclimatized man. With acclimatization, cellular changes affecting oxygen utilization give protection, but serious signs of impaired functions, e.g., disturbances of vision, partial paralysis, and other signs of nervous failure, have not been infrequent on mountains when men are driving their muscles to the limit, showing that the danger point had been reached.

Matthews, D.S., and B. Tribed. Some effects of high altitude climbing: investigations made on climbers of the British Kangchenjunga Reconnaissance Expedition, 1954. Brit. Med. J. 4916:768-769 (26 Mar. 1955). Assessments were made of the physiological changes which occurred at high altitudes in climbers participating in the 1954 British Kangchenjunga Reconnaissance Expedition. Some general clinical observations were made on the circulatory and respiratory responses to acclimatization, the effects of high altitude on the eyes, vision, body fluids (including blood and urinary electrolytes), behaviour and mental processes, and sleeping habits.

Magdalena, F. M. A study of post-hypoxic paradox effect. Presented at the thirty-fourth Annual Meeting, Aerospace Medical Association, 1963. Abstract *in* Aerospace Med. 34(3):260 (1963).

Maurath, J., and P. Hauer. Acid-base equilibrium and respiratory regulation in chronic hypoxemia. Klin Wschr. 30(1344):315-319 (1 Apr. 1952). The following observations were made on patients with chronic hypoxemia caused by pulmonary insufficiency: inhalation of oxygen caused complete vascular oxygen saturation, an increase of plasma carbon dioxide, and a corresponding decrease in pH, a decrease in pulmonary ventilation, and an increased ability of the arterial blood to combine with CO_2; this abnormality ceases upon termination of the anoxic stage. The kidney was observed to act in a compensatory capacity (increase of alkali reserve) upon extensive inhalation of O_2. The physiological mechanism of the observed phenomena is discussed.

Maurer, F. W. Effects of decreased blood oxygen and increased blood carbon dioxide on flow and composition of cervical and cardiac lymph. Amer. J. Physiol. 131:331 (1940).

Mazurenko, T. I. Certain adaptive reactions of the organism in hypoxic states in hypertonia patients. AFSC N65-17795, Foreign Technology

Div., Wright-Patterson AFB, Ohio. Observations of hypertonic patients are reported. Gas composition of the blood hemoglobin content, erythrocyte count, diameter, volume, and thickness and number of reticulocytes were measured. The oxygen index to hemoglobin capacity was calculated. It was observed that a drop in the oxygen capacity of the hemoglobin accompanied the increase in its amount, and that a subsequent drop in the amount of hemoglobin was accompanied by a rise in its oxygen capacity. Variability observed in the indices of hemoglobin-oxygen capacity and the variation of the erythrocyte composition of the blood represent compensatory mechanisms of the organism.

Mazza, S. and A. Bianchi. Comparative studies of blood of some persons at altitudes of 1200 and 3500 meters. Bol. Hist. Clin. Quir. 4:454-460 (1928).

Mazza, M. A. Adaptation of soldier to mountains. Dia Med. 13:162-167 (10 March 1941).

Mazzotti, L., and J. Ramirez. Investigation of oxyuriasis in 813 individuals of Mexican plateaus. Salub. Y Asist. 1(-111):114 (Jan.-Feb. 1944).

McDonald, R. K., and V. C. Kelley. Effects of altitude anoxia on renal function. Amer. J. Physiol. 154:193-200 (Aug. 1948).

McFarland. Psycho-physiologic studies in Andes: sensory and circulatory responses of Andian residents at 17,500 feet. J. Comp. Psychol. 24:189-220 (Aug. 1937).

McFarland. Psycho-physiologic studies in Andes: mental and psychosomatic responses during gradual adaptation. J. Comp. Psychol. 24:147-188 (Aug. 1937).

McFarland, R. A., F. J. W. Roughton, M. H. Halperin, and J. I. Niven. The effects of carbon monoxide and altitude on visual thresholds. Aviation Med. 15:381-394 (Dec. 1944).

McFarland, R., and D. B. Dill. Comparative study of effects of reduced oxygen pressure on man during acclimatization. J. Aviation Med. 9:18-44 (Mar. 1938).

McGinty, D. A., and R. Gesell. On the chemical regulation of respiration: II. A quantitative study of the accumulation of lactic acid in the isolated brain during anaerobic conditions and the role of lactic acid as a continuous regulator of respiration. Amer. J. Physiol. 75:70-83 (1962).

Meda, E. Basal metabolism in acclimatization to high altitude. Bol. Soc. Ital. Biol Sper. 31(1-2):37-38 (Jan.-Feb. 1955). Persons living at high altitude (3000 meters) in Col d'Olen, Italy, for 7 to 17 days exhibited no appreciable change in oxygen consumption during acclimatization in comparison to values obtained at sea level. No change was noted in carbon dioxide elimination as calculated by the respiratory quotient. The respiratory quotient was not significantly modified (average value at sea level, 0.853; at high altitude, 0.837). A slight variation in the basal metabolism was demonstrated.

Mefferd, R. B.: High altitude research J.A.M.A. 156(6):626-627 (9 Oct. 1954). This letter briefly summarized a review contained in the 1952-1953 Annual Report of the Medical Research Council of Great Britain concerning the preparations made for Sir John Hunt's conquest of Mt. Everest in 1953. Experience on earlier expeditions had indicated that direct ascent to high altitude would have deleterious effects (incapacitating exhaustion, diarrhea, upper respiratory infections), and it was, therefore, recommended that members of the 1953 expedition should spend a month in the Himalayas to become acclimatized and to pass through the stage of initial infections before beginning the ascent of the mountain. While climbers wore their masks for part of each day on the approach march, trial ascents were made with both open and closed circuit oxygen sets. They also learned to sleep comfortably wearing a light BOAC mask and breathing one liter of O_2 per minute. A flow rate of two liters of O_2 per minute was found adequate for descent and for the second man on the rope during ascent, but four liters were needed by the leader while cutting steps or making tracks. Work rate was not significantly improved by the use of oxygen up to 22,000 feet, but above this altitude the improvement in climbing rate became increasingly evident. At all altitudes above 18,000 feet, endurance was greatly enhanced. Breathing was easy, there was less sense of effort, and fatigue at the end of the day was markedly diminished. More prolonged exertion was possible in a day with the help of oxygen than without it. Oxygen at night induced warmth and sleep and provided recovery from fatigue. Provisions for food rations, protective clothing, and equipment are also described.

Mefferd R. B., and H. B. Hale. Effects of altitude, cold, and heat on metabolic interrelationships in rats. School of Aviation Med., AD 149 556, Randolph AFB, Texas, (1957). Adult male Wistar rats were exposed for three months either to simulated altitude or to hot or cold environments, and comparisons were made during the final

month, these comparisons included body weight, food and water intake, and the 24-hour fasting urine volume and the excretion of sodium, potassium, phosphate, magnesium, calcium, urea, uric acid, creatinine, taurine, histidine, glycine, alanine, valine, aspartic acid, glutamic acid, methionine, and serine. Correlational analyses showed that many of the above listed variables remained constant in the different environments regardless of the extent of quantitative changes. Intergroup changes in the variable relationships noted in certain of these environments may indicate either an incomplete acclimatization or an environmentally specific adaptation.

Mefferd, R. B., and H. B. Hale. Effects of altitude, cold, and heat on metabolic interrelationships in rats. Amer. J. Physiol. 193:-443-448 (1958).

Mefferd, R. B., and H. B. Hale. Effect of thermal conditioning on metabolic responses of rats to altitude. Amer. J. Physiol. 195:735-738 (1958).

Megel, H., H. Wozniak, E. Trazier, and H. C. Mason. Effect of altitude upon tolerance of rats to vibration stress. Aerospace Med. 34(4):319-321 (April 1963). Restrained adult male rats of a Sprague-Dawley

strain were exposed to sinusoidal or random vibration at varying simulated altitudes. Using mortality as the index of tolerance, exposure of animals to sinusoidal vibration and altitudes less than 10,000 feet results in incidences of mortality which did not differ from that observed for vibration at sea level. Above 10,000 feet, mortality percentage increased as a function of altitude. The increased mortality resulting from simultaneous exposure to the combined environments may be attributed to the effects of reduced partial pressures of oxygen. Exposure of restrained rats to the combined environments of random vibration and an altitude of 18,000 feet resulted in interaction with regard to mortality. Pulmonary hemorrhage was found in those animals succumbing to the combined environments.

Mei-Lei. Change in the dynamics of the formation of electric reactions of the visual analysor in the presence of hypoxia. Foreign Tech. Div., AD 286 102 Air Force Systems Command, Wright-Patterson Air Force Base, Ohio.

Meneses Hoyos, J. Cardiac output in persons acclimated to the altitude of Mexico City (2240 meters above sea level) is not appreciably higher than that of inhabitants of lower levels. Med. Rev. Mex. 37(780): 429-444 Sept. 1957. Normal values for blood circulation were

determined in inhabitants of Mexico City (7345 feet altitude). Results showed that the characteristics of blood circulation were the same as those found in persons living at sea level, with minor differences in erythrocyte number, hematocrit, hemoglobin concentration, and total volume of circulating blood. These differences, although slight, were enough to explain altitude acclimatization. Cardiac output did not appear to increase in inhabitants of Mexico City.

Meranda, A., and A. Rotta. Measurements of heat of native and long-time residents: preliminary report. <u>An. Fac. Med.</u> (Lima) 26:49-58 (1944).

Merayo, F. M., and J. Ruiz-Gijon. A study of post-hypoxic paradox effect. Presented at thirty-fourth Annual Meeting of the Aerospace Medical Association, Los Angeles, California, 29 April - 2 May 1963. Investigators are not in agreement on the etiology of the post-hypoxic effects provoked by inhalation of O_2. Many authors relate the respiratory inhibition to the decrease of the alveolar pCO_2 produced by hyperventilation. The French authors attribute the preponderance of the effect to O_2 in the production of this apnea. The evidence presented contradicts the findings of investigators who

consider it to be the result of hypocapnia. Three types of experiments were performed: on normal animals, on animals which had carotid sinuses destroyed, and on animals which had been given a mixture of N_2 and CO_2 in variable proporations (from 3 to 10 percent) during the anoxic phase.

Mercier, A., and J. Moracchini. Behavior of heterophorias at high altitude. Bull. Soc. Ophtal. (France.) 1076-1077 (Dec. 1949).

Merckie, H., and E. Opitz. Blood vessels of pia mater in rabbits adapted to altitude. Arch. Ges. Physiol. 251:117-122 (1949).

Merckie, H., and M. Schneider. Capillary changes of the brain during adaptation. Arch. Ges. Physiol. 251:49-55 (1949).

Merino, C.F. The plasma erythropoietic factor in the polycythemia of high altitudes: Preliminary Report, School of Aviation Med., AD 126283, Randolph AFB, Texas. An investigation was made of the possible presence of an erythropoietic factor in the plasma of native residents at high altitude (between 3900 and 4540 meters). The injection of 250 to 300 cc. of plasma obtained from these men into 15 healthy subjects living at sea level resulted in a moderate but constant increase of reticulocytes, which reached its maximal degree between the second

and fourth day after the injection. The constancy of this finding and the absence of response in another group of 13 men who received plasma from sea-level residents gives some significance to the data obtained.

Merino, C.F., and C. Reynafarje. Bone marrow studies in polycythemia of high altitudes. J. Lab Clin Med. 34:637-647 (May 1949). Studies were made of the bone marrow of sixteen healthy Indian adults, permanent residents in Cerro del Paseo (Peru) at an altitude of 4390 meters (14,400 feet). Samples were obtained by means of sternal aspirations, and supravital and Wright stained preparations were used for the qualitative as well as quantitative microscopic examinations. All men showed a definite polycythemia in the peripheral blood. The results obtained were compared with previous observations made on healthy people living at sea level and in patients with polycythemia vera.

Merino, C.F. Mechanism of polycythemia. Gac. Med. (Lima) 1:69-70 (Dec. 1944).

Merino, C.F. Studies on blood formation and destruction in the polycythemia of high altitude. Blood 5:1-31 (1950). Studies of blood formation and destruction in the polycythemia of high altitude have been carried out. Three different groups of subjects were studied: (1) Healthy adult male subjects from sea level who, after being studied at this level, were taken to an altitude of 4540 meters (Morococha) where they developed a marked polycythemic process. When these subjects returned to sea level, the mechanisms of recuperation of the hematologic equilibrium were studied. (2) Normal adult subjects, native of high altitude, chronically polycythemic due to their permanent residence in Morococha, who were first studied in their native town and then brought to sea level where they were observed during five weeks. (3) Subjects, residents of high altitude (Morococha), who had lost their adaptation i.e., who had developed chronic altitude sickness or Soroche (Monge's malady).

Meschia, G. Oxygen dissociation curves of the bloods of adult and fetal sheep at high altitudes. Jour. Exper. Physiol 46 (2): 156-160 (April 1961). The O_2 dissociation curves of the blood of adult and fetal sheep living at an altitude of 14,000 feet in Morococha, Peru, were prepared at plasma hydrogen-ion concentrations in the physiological range. A comparison with oxygen-dissociation curves of the blood of sea-level sheep and their fetuses showed no significant difference between the two groups of animals.

Metz, J., N. W. Levin, and D. Hart. Effect of altitude on the body-venous hematocrit ratio, Nature 194:483 (5 May 1962). The concentration of red cells is not the same in all parts of the circulatory system, the cell-plasma ratio being lower in the capillaries and small vessels than in the larger arteries and veins. The overall cell percentage (body hematocrit) is determined from the direct measurement of both red cell volume and plasma volume, and from this the body-venous hematocrit ratio (BH/VH ratio) is calculated. In normal adult residents at sea level, the BH/VH ratio averages 0.91.

Meyez, K., and A. Staffe. Catalase and Altitude. An. Soc. Biol. (Bogota). 6(3):94-108 (Feb. 1954). Blood catalase levels of humans and rabbits living in Bogota, Colombia (2640 meters altitude), are 60 percent higher than in subjects living at Gerardot, Columbia (326 meters above sea level). The change cannot be related to blood O_2 content or to the number of erythrocytes. It is suggested that a catalase inhibitor is active at low altitudes and inactive at high altitudes. It is also noted that blood catalase content increases during aircraft takeoff and decreases upon landing. These changes appear suddenly.

Michal, C., et al. Metabolic changes in heart muscle during anoxia. Amer. J. Physiol. 197 (6) 1147-1151 (1959). The studies reported deal with the effects of varying periods of complete myocardial anoxia on the concentrations of reduced and oxidized diphosphopyridine nucleotide, reduced and oxidized triphosphopyridine nucleotide, elycogen, edenosine triphosphate, hexose monophosphate, phosphorcreatine and inorganic phosphorus in heart muscles. Oxygen lack leads to rapid dephosphorylation of high energy phosphate components and to the formation of inorganic phosphorus. The decline of adenosine triphosphate in heart muscle was more rapid than the diminution in the Q_{O_2} of heart muscle slices as reported in earlier works. There was considerable glycogenolysis. The rate of glycogen breakdown did not appear to depend upon the amount present in heart muscle until very low levels were reached. Prior to the onset of anoxia, most of the diphosphopyridine nucleotide was in its oxidized form. The oxidized diphosphopyridine nucleotide and reduced triphosopyridine nucleotide decreased with time, while reduced diphosphopyridine nucleotide increased. The total concentration of diphosphopyridine nucleotides in heart muscle diminished.

Michel, C.C., and J.S. Milledge. Respiratory regulation in man during acclimatization to high altitude. J. Physiol. (London) 168:631-643 (Oct. 1963). Respiratory response to combinations of hypoxia and hypercapnia was studied in four healthy male subjects at sea level during and after acclimatization at 19,000 feet. Responses were compared by using the equation of Lloyd, et al., which related pulmonary ventilation to the alveolar pO_2 and alveolar pCO_2. It was found that the parameters related to hypoxia were slightly affected by several months at high altitude, while the parameters of the hypercapnic response were conspicuously changed.

Michel, E. D., and T. K. Cureton. Effects of physical training on cardiac output at ground level and at 15,000 feet simulated altitude. Res. Quart. 24:446-452 (Dec. 1953). This study was conducted to show the effects of training on the cardiac output during a training program and to see if any changes made would be reflected in the reaction of the body to the stresses of high altitude.

Michel, T. E., R. W. Langevin, and C. F. Gell. Effect of continuous human exposures to oxygen tension of 418 mm. Hg for 168 hours. Aerospace Med. 31:138 (1960). An investigation was carried out which indicated that the inhalation of oxygen at a partial pressure of 418 mm. Hg for a period of 7 days was without marked effect on the general appearance, activity, and physical well-being of six healthy men. The following signs of pulmonary irritation which occurred during these studies indicate that the limits of human tolerance to higher-than-normal oxygen concentration may have been approached; substantial tightness, decrease in vital capacity in two subjects, and the occurrence of an area of probable atelectasis in one subject.

Mikhnev, A. L., and N. S. Zanozdra. AFSC N65-17792, Foreign Technology Div., Wright-Patterson AFB, Ohio. Patients suffering from atherosclerotic myocardiosclerosis were studied; their external respiration indices, gas content of the arterial and venous blood, oxyhemoglobin dissociation, and carbonic acid fixation were determined. Increase in respiratory frequency indicated that the external respiratory apparatus was operating under stress, and decrease in depth and reserve of respiration and the respiratory coefficient indicated its relative inadequacy. Carbon dioxide in the venous and arterial blood increased when pneumosclerosis was present. A decrease was noted in persons with circulatory insufficiency and myocardiosclerosis. An upward and left shift of the oxyhemoglobin dissociation curve was noted for a patient suffering from manifest pneumosclerosis, pulmonary emphysema, and pulmonary cardiac insufficiency. A shift right and downward indicated, in some cases, circulatory insufficiency.

Miles, S. The effect of changes in barometric pressure on maximum breathing capacity. J. Physiol (London) 137(3):85-86 (6 Aug. 1957). Mountaineers find that as altitude increases, the air, being less dense, offers less resistance to breathing. It would, therefore, seem logical to expect a corresponding reduction in MBC with increased pressure.

With pressures of 2, 3 and 4 atmospheres, mean decreases in MBC from sea level value were found to be 27.3 ± 1.6, 41.1 ± 2.3 and 48.2 ± 1.9 percent respectively.

Milledge, J. S. Electrocardiographic changes at high altitude. Brit. Heart J., 25(3):291-298 (May 1963). Serial electrocardiograms were taken during the 1960-1961 Himalayan Scientific and Mountaineering Expedition on climbers who spent approximately 5 months at 19,000 feet. There was a shift of direction of the QRS and T vectors to the right in the frontal plane. In the precordial leads, there was a shift to the left of the transitional zone of the QRS-complex and inversion of the T wave spreading across from right to left (from VI-2 to V4-5), i.e., a backward shift of the QRS and T vector in the sagittal plane. Oxygen breathing did not reverse these changes except in the first oxygen experiment. A decrease was observed in the amplitude of the QRS voltage which was reversed by oxygen breathing. The cardiogram at altitude showed unmistakable signs of right ventricular overload, but the most significant finding was that the cardiograms of men at altitudes as high as 24,400 feet showed little evidence of the severe physiological stress under which there were working. Included are representative electrocardiograms and tables.

Milledge, J.S. Respiratory regulation at 19,000 feet (5700 meters). In Cunningham, D. and B. Lloyd (ed.) The regulation of human respiration, pp. 397-407. Oxford: Blackwell Scientific Publications.

Miller, S.U. Increased human body water loss at reduced ambient pressure. Aerospace Med. 22(6):689-691 (June, 1962). The observed phenomenon of increased human body water loss at reduced ambient pressure is reported, and a theoretical hypothesis to explain the phenomenon provided. The significance of this finding relative to closed environmental systems and to clinical medicine is discussed.

Miranda, A., and A. Rotta. Measurements of the heart of native and long time residents: preliminary report. Am Fac. Med. (Lima) 26:49-58 (1944).

Mirrakhimov, M.M. Data on acclimatization to the mountain country of Kirgiz. AFSC N65-17189, Foreign Technology Div., Wright-Patterson AFB, Ohio. Adaptation to high altitudes (1500 to 1800 meters) in the Kirgizia region for a long period of time led to changes in certain functions of the organism, such as those of the cardiovascular system, which became adjusted to more efficient utilization of oxygen. The gas exchange level became lower. The hemoglobin concentration was higher, although the red blood count remained normal. Pulse rate,

arterial pressure, and blood flow rate decreased. Venous pressure, capillary permeability, and pulmonary circulation showed an increase. A general depression in body function level was evident. Under such circumstances, the minute cardiac volume, an indicator of hemodynamic activity, remained normal.

Mise, J., and Y. Hitsumoto. Mechanics of breathing in low or high oxygen and high carbon dioxide inhalation. Presented at the twenty-sixth Annual Meeting of the Japanese Circulation Society, 1962. Abstract in: Japanese Circulation J. 26(11)872 (1962).

Mito, A. Studies on right ventricular overloading during induced anoxia with the use of double lumen catheter. Japanese Circ. J. 27(1): 47-50 (1963). A double lumen catheter was employed to examine the hemodynamics of the right heart. Also the factors which cause pulmonary hypertension in anoxia were determined. The relationship between the heart sound and the intersecting point of the ventricular and arterial pressure curves was as follows. the second sound and the closing point of the pressure curve coincided well; the first sound did not coincide well with the opening point of the curve. Differences were probably due to interference of sounds due to blood flow, myocardial vibration, etc. When the pulmonary artery pressure rises (including induced anoxia) the effective expulsion time of the right ventricle shortens, and the ventricle is forced to expel a certain amount of blood within a short time. In cases with no obstruction in blood flow, the pressure difference between the systolic right ventricular and pulmonary pressures decreases as the mean pulmonary arterial pressure rises. Thus, the right ventricle is placed in a state of an increased pressure load. When the state becomes more severe, the possible occurrence of right ventricular insufficiency can be predicted.

Miyachi, K. Information on human skin temperature on a plâteau (effect of hot and cold baths). Far East Sci. Bull. 2:43 (June 1942).

Miyahara, M. et al. Studies on the metabolism of phosphate compounds in the heart; I. Distribution in the normal heart muscles; II. Changes in the anoxic heart muscles. Presented at the Annual Meeting of the Japanese Circulation Society, 1962. In: Japanese Circulation J. 26 (11): 903-904 (1962).

Moffatt, D.S. The effect of hypoxia on guinea-pig bone marrow. J. Physiol. 127(2): 48P-49P (July 1961). Seventy-five guinea pigs were exposed to a simulated altitude of 14,000 feet at room temperature for 5 days (primary hypoxia) taken out for 5 days (rebound), and resubmitted for an additional 5 days (secondary hypoxia). Five animals per day were sacrificed and their bone marrow analyzed by Yoffey's quantitative technique. There was an overall rising tendency in the total nucleated cell count during primary and secondary hypoxia and a falling tendency during rebound. Marrow lymphocytes fell throughout primary hypoxia but rose again during rebound and secondary hypoxia to nearly 100 percent above the control level. Granulocytes in the blood and bone marrow showed no changes. The blood showed varying degrees of polycythemia throughout an experiment, with peaks during the hypoxic phases. It is concluded that the lymphocyte plays an important role in erythroid hyperplasia.

Moncloa, F. Studies of urinary steriods in men born and living at high altitudes. Proc. Soc. Exp. Biol. 108 (2): 336-337 (Nov. 1961). Urinary excretion of steriods was studied in men born at 10,000 feet and living at 14,900 feet, and in men born and living at sea level. No differences were found between the groups in urinary excretion of steriods, cortisol catabolism, or the effect of inhibition of endogenous ACTH by Dexamethasone administration on urinary steroid excretion.

Monge, C. Chronic mountain sickness. Physiol. Rev. 23:166-184 (Apr. 1943).

Monge, C. Disease of Andes or erythremia. Rev. Sudam. de Me'd. et de Chir. 1:825-831 (Aug. 1930).

Monge, C. C., et al. A description of the circulatory dynamics in the heart and lungs of people at sea level and at high altitude by means of the dye dilution technique. Acta Physiol. Lat. Amer. 5(4):198-210 (1955). The circulatory dynamics of the heart and lungs of subjects living at high altitude (14,900 feet) and at sea level were determined by the dye dilution technique. Values for circulation time, cardiac output, intrathoracic blood volume (calculated by Hamilton formula), lung blood volume, and lung blood volume, compared with total blood volume, were increased slightly in 10 male Peruvian natives living at high altitude, over values obtained from 20 male and 20 female subjects living at sea level.

Monge, C. Acclimatization in the Andes, Brown, D.F. (ed). Baltimore: John Hopkins Press, 1948.

Monge, C.M. Acclimatization in the Andes. An Fac. Med. 43(2):165 (1960). A bibliography containing 528 references with abstract, author, and subject indices pertaining to studies on the physiology of acclimatization to the high altitudes of the Peruvian Andes. Investigations of mountain sickness are also included.

Monge, C. Biologic characteristics of man in the Andes. Bol Acad Nac. Med. (B. Air.) pp. 695-721 (Nov. 1934).

Monge, C. Man, climate, and change of altitude: Recent studies on bioclimatology. An. Fac. Med. (Lima) 37(3):459-485 (1954). Bioclimatological studies were made on persons living at high altitudes in Montana, Peru. The process of acclimatization in persons living in the Andes is reviewed, and the physio-pathological aspects of high-altitude hypoxia which leads to altitude sickness in persons adapted to high altitudes are noted, along with the physiological manifestations (cardiac, pulmonary, hematological) in these persons, who, upon their return to sea level, showed a marked physical deficiency and a predisposition to pathological respiratory processes. It is concluded that climatic aggression in acclimatized man leads to the loss of his acclimatization and ultimately to altitude sickness.

Monge, C. The concept of acclimatization. An. Fac. Med. (Lima) 38(1):1-8 1955. A brief review is presented of the concept of acclimatization to high altitudes with reference to congenital or acquired acclimatization. It is noted that when congenital or acquired acclimatization is lost, chronic mountain sickness follows which may be cured by descent to lower altitudes or to sea level. The two types of mountain sickness are: a type permitting man to live and reproduce, eventually leading to acclimatization (racial acclimatization), and a type whereby man lives normally but cannot reproduce (individual acclimatization). This latter type is exceptional and can be cured by descent to lower altitudes or to sea level.

Monge, C. Life in the Andes and chronic mountain sickness. Science 95:79-84 (23 Jan. 1942).

Monge, C. Vegetative nervous system of men of Andes. J. Neuro-Psiquiat Panam. Acta 2:56-67 (1939).

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Monge, C. Biologic and clinical syndrome caused by changes in altitude. Bull. Schweiz Akad. Med. Wiss. 7:187-197 (July 1951).

Montemartini, C., V. Baldrighi, A. Marchesi, and L.G. De Carlo, Jr. The behavior of venous pressure and circulation time in induced hypoxia and hypercapnia. Atti. Soc. Ital. Cardiol. 22(2): Comunicazioni 429-30 (1962).

Mookerjee, M.K., and S.K. Dargupta. Variation of blood glucose in man at simulated altitudes between 10,000 and 30,000 feet in decompression chamber. Aero Med. Soc. J. (New Delhi) 1(2):37-40 (Oct. 1954). This investigation assessed the influence of reduced barometric pressure on blood-glucose levels and attempted to correlate the variations of blood glucose levels, if any, with the onset of flying fatigue at altitudes between 10,000 and 30,000 feet. Blood sugar determinations were made on

four subjects after breakfast, every 1/2 hour for 2-1/2 hours at ground level. Further observations were carried out at altitudes of 5,000, 10,000, and 15,000 feet, at the base on arrival and 1/2-hour afterwards. Twelve subjects were exposed to simulated altitudes from 15,000 to 30,000 feet. Glucose tolerance tests were carried out on six subjects at ground level and compared with blood sugar levels at 20,000, and 25,000 feet on the following day. An analysis of the results showed wide individual variations of blood-sugar levels, but in none of the individuals did the blood-sugar levels indicate hypo- or hyperglycemia. A comparison of tolerance curves showed that return of blood-sugar levels to pre-ingestion values occurred at approximately the same time, both on the ground and at simulated altitudes. It was concluded that there was no significant change from ground-level condition in the blood-sugar levels of resting human subjects maintained at simulated altitudes of 10,000 to 30,000 feet if oxygen was used.

Mookerjee, G. C., and D. K. Ghose. Life and cold and altitude: some observations. Armed Forces Med. J. (India) 9(1):1-11 (Jan. 1953). Observations are presented on some of the physiological changes taking place during exposure to a typical cold winter in the Himalayan ranges of India at altitudes between 6,800 and 11,000 feet. The medical and physiological problems covered include body temperature, respiration

at altitude, hematological changes, cardiovascular reserve, nutrition and caloric requirements, body weight changes during residence at altitude, and basal metabolism during work. Criteria for selec- suitable subjects for service at high altitude are centered around these four factors; low basal pulse rates, difference between standing and lying pulse rate less than 20 beats per minute, normal blood pressure, and a high Harvard Pact Test score.

Moore, C. R., and D. Price. Study at high altitude of reproduction growth, sexual maturity, andorgan weights. J. Exp. Zool. 108:171-216 (July 1948).

Mori-Chavez, P. Spontaneous leukemia at high altitude in C58 mice. J. Nat. Cancer Inst. 21(5):985-997 (Nov. 1958).

Morikofer, W. Characteristics and evaluation of the high-mountain climate. Med. Mschv. (19):642-645 (1953). The therapeutic advantages of high mountain climate are discussed. During the warmer seasons, the intensity of moderate ultraviolet radiation (UV) is approximately 1-1/2 to 2 times greater at 1600 meters than at sea level, and 3 to 4 times greater in winter than in summer. The increase in UV intensity for 100 meters elevation is about 3 to 10 percent in summer and 10 to 20 percent in winter. Insolation and radiation intensity increase

with altitude, while the temperature of the air decreases. The result is a cooling effect which has a stimulating influence on the heat regulation mechanism of the body. Absolute atmospheric humidity decreases. Decreases of air pressure and oxygen content up to altitudes of 2000 meters cause an increase of respiratory rate and depth and erythrocyte production.

Morisi, V. Therapeutic qualities of high-altitude air. Bull. Sci. Med. (Bologna) 121:13-21 (Jan.-Mar. 1949).

Morton, W. E., D. J. Davis, and J. A. Lichty. Mortality from heart disease at high altitude. Arch Environm. Health (Chicago) 9:21-24 (July 1964). Since practicing physicians in Peru and Colorado have suggested that fatal cases of coronary thrombosis and hypertension were rare at higher elevations, Colorado mortality statistics (1949 to 1951 and 1959 to 1961) for these causes were analyzed for variation by altitude. Altitude-associated variations in crude cause-specific mortality rates were eradicated by age-standardization of the rates, indicating that the apparent scarcity of fatal cases of arteriosclerotic heart disease and hypertension at high altitude in Colorado is due to the smaller proportion of older persons in the population. There is no increased mortality risk from these causes at higher elevations in Colorado despite the existence of altitude-induced erythremia.

Moss, Arthur J. The effect of hypoxia on the rate at which the cardiac ejection force is generated: A ballistocardiographic study. Naval School of Aviation Med. Res. Proj. NM 18 03 11, Sub task 6, Report No. 5:1-24 (1959). A relative value for the rate at which cardiac force is generated can be obtained from the slope of the ejection deflection on the acceleratory ballistocardiogram. A standard hypoxic stress (10-percent oxygen for 20 minutes) significantly increased the rate of cardiac ejection in each of the 6 normal subjected studied -- some to a greater degree than others. These changes with anoxia give a further understanding of the origin of the ECG deflections, and, in addition, reveal new information about cardiac stress.

Motley, H. L., et al. The influence of short periods of induced acute anoxia upon pulmonary artery pressures in man. Amer. J. Physiol. 150:315 (1947).

Mouriquand. Acclimatization of children in mountains. Gaz. Med. France (supp. Climat. d'été): 27-30 (1 June 1935).

Müller, F. Action of high altitudes on man. Deutsch Med Wschr. 52:1541-1542 (10 Sept. 1926).

Muller, B. The influencing of altitude tolerance by increasing the body temperature. Z. Flugwissenshaften (Braunschweig) 1(5): 131-136 (Oct. 1953). Experiments were conducted to determine the effect of an increase in body temperature on the resistance to altitude sickness. Artificial fever in the range of 38 to 39.4°C was induced in normal healthy subjects by injections of a fever-producing drug, "Artizon". A rebreathing apparatus permitting oxygen tension of approximately 5000- to 6500-meter altitude was used to simulate high-altitude environment. An increase of body temperature up to 38°C did not significantly lessen altitude tolerance which was compensated for by an increased blood flow and by hyperventilation. On the contrary, a slight tendency to an increase in the resistance of the organism to altitude sickenss was observed. At higher-body temperature (above 38°C), an unmistakable decrease in altitude tolerance was noted. The increases in minute volumes and hyperventilation were insufficient to maintain the oxygen hemoglobin concentration which was manifested in a premature onset of altitude deterioration. The experiment also confirmed the previous observation that an increase in blood temperature at decreased oxygen partial pressure, i.e., at increased altitude, acts as a decreased saturation of the hemoglobin.

Muralt, G. von, and W. Hirsigu. Prothrombin level of human blood in high-mountain climate. Helv. Physiol. Pharmacol Acta 6:626-638 (1948).

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Muralt, G. von, and A. Stettler. Behavior of blood cholinesterases in high-mountain climate. Helv. Physiol. Pharmacol. Acta 6:663-673 (1948).

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Naar, A.B. Physiopathology: Hemopoietic phenomena and acclimatisation dyshidrosis on descending. Med. Cir. (Bogata) 6:245-252 (Feb. 1942).

Nadel, J.A., and J.G. Widdecombe. Effect of changes in blood gas tensions and carotid sinus response on tracheal volume and total lung resistance to air flow. J. Physiol. (1962), 163:13-33. To study the reflex responses in the airways, changes in volume of a segment of the trachea and total lung resistance to air flow were simultaneously measured in anaesthetized dogs that were paralysed and artifically ventilated. Inhalation of 10 to 15 percent O_2 in N_2 or injection of small doses of nicotine into a common carotid artery caused constriction of the upper and lower airways. Constriction was prevented either by tying the glossopharyngeal nerves (which supply the carotid chemoreceptors) or by cooling the cervical vagosympathetic nerves. It is believed that the response is due to stimulation of carotid body chemoreceptors. Inhalation of 2 to 8 percent CO_2 in room air caused constriction of upper and lower airways which was prevented by cooling the vagosympathetic nerves, but not by tying the glossopharyngeal nerves. The site of action of CO_2 was not further localized. The size of the response of the airways depended on the degree of hypoxemia or hypercapnia. Elevation of blood pressure in perfused carotid sinuses caused a small but significant dilation of the trachea, although there was no significant change in total lung resistance. A decrease in pressure caused a tracheal constriction. The responses were abolished by tying the glossopharyngeal nerves or by cooling the vagosympathetic nerves. The effects are believed to be due to carotid sinus baroreceptors.

Naeye, R. L. Hypoxemia effects on the [anatomy of the] pulmonary vascular bed. Presented at the Fifty-fourth Annual Conference on Research in emphysema: normal and abnormal pulmonary circulation, 1962. Med. Thorac. (19(5):494-501 (1962). Chronic hypoxemia has often been noted to increase pulmonary vascular resistance. The current study demonstrates associated structural changes in the pulmonary vessels of human beings and mice, including hypertrophy of smooth muscle about the small muscular arteries, extension of smooth muscle to some small precapillary vessels which ordinarily do not have a muscular coat, and dilation of pulmonary arteries and capillaries. It is postulated that all of these structural changes contribute to the increased pulmonary vascular resistance.

Nagaki, H., S. Hayashi, S. Miyagawa, and S. Lamakura. Studies on the experimental myocardial infraction by the ligation of the coronary artery and hypoxia in dogs. Presented at the Twenty-Sixth Annual Meeting of the Japanese Circulation Society, 1962. Abstract in Japanese Circulation J. 26(11):907 (1962).

Nahas, G.G. Pulmonary effects of rapid changes in oxygen tension. A. Influence of hypoxia on the pulmonary circulation of non-narcotized dogs. AF School of Aviation Med., AD102690, Randolph, AFB, Texas (Jan. 1955). Methods are described for measuring intracardiac pressures and "cardiac output" in the normal, trained, non-narcotized dog, breathing eight percent oxygen in nitrogen (hypoxia). Under these experimental conditions, the following respiratory and circulatory changes were observed: an increase in integrated mean pulmonary artery pressure; no significant change in left arterial pressure; a trend toward an increase in heart rate; and an increase in cardiac output, measured five minutes after hypoxia by the dye-dilution method; and pulse measurements taken over a five-minute period beginning five minutes after onset of hypoxia.

Nahas, G.G., et al. Pulmonary effects of rapid changes in oxygen tension. B. Influence of acute hypoxia on the pulmonary circulation of

sympathectomized and adrenalectomized dogs. AF School of Aviation Med., AD 102690, Randolph, AFB, Texas (Jan. 1955). In five sympathectomized, nonnarcotized dogs exposed to eight percent oxygen in nitrogen, the changes in heart rate and cardiac output were of smaller magnitude than in intact animals. In five adrenalectomized dogs studied under the same conditions these changes were not present.

Naitore, A. Effects of hypoxia and hypercapnia on gastric acid secretion in man. Gastroenterology 43(2):181-188 (Aug. 1962). The separate and interacting effects of alveolar carbon dioxide and oxygen tension on gastric acid secretion were studied in normal humans exposed to a variety of gas mixtures at sea level and at high altitude (14,246 feet). Acid secretion following the test meal was, in general, directly related to alveolar carbon dioxide tension. Moreover, the amount of acid secreted at any given carbon dioxide tension was found to increase as the accompanying oxygen tension decreased. However, elevation of carbon dioxide tension did not affect fasting secretion in man. It is concluded that changes in carbon dioxide and oxygen tensions can significantly modify an existing state of acid secretion, but this modification cannot be universally demonstrated in all types of secretory studies. A discussion is included on the possible role played by changes in gastric blood flow in determining the gastric secretory responses.

Nayak, K.K., O.P. Milhotra, and G. Kupperswany. Pulmonary edema of high altitude. Armed Forces Med. J. (India) 18(4):546-551 (Oct. 1962). Eight cases are reported of pulmonary edema observed at high altitudes. Pulmonary edema occurs in apparently healthy but unacclimatized and susceptible individuals within 8 to 48 hours after exposure to altitude (9300 feet and above). It is characterized by breathlessness at rest, cough, hemoptysis, trachycardia, and rales. These symptoms regress within 24 to 48 hours after removal to a lower altitude or administration of oxygen. The condition is liable to recur upon re-exposure to high altitude and to end fatally. Acclimatized mountain residents are liable to pulmonary edema when they descend to the plains temporarily and then return to high altitude. The etiology of pulmonary edema is unknown, but hypoxia at high altitude may possibly either stimulate or inhibit the pituitary, depending upon whether exposure to hypoxia is slow and gradual or immediate. A gradual acclimatization at lower altitude before going to high altitude is suggested as a preventative measure. Unacclimatized persons should carry portable oxygen apparatus and inhale oxygen on the appearance of breathlessness and cough at rest.

Nazarenko, A. I. On the role of the hypoxic factor in the development and course of experimental epileptic seizures. AFSC·N65-17841, Foreign Technology Div., Wright-Patterson AFB, Ohio. The functional state of the respiratory and circulatory systems of dogs was studied to determine the role of hypoxia in the genesis of convulsive seizures. It was observed that respiration and blood pressure vary considerably during convulsive seizures. In the tonic phase, a sharp increase in blood pressure takes place and respiration stops. At the peak of the seizure, the oxygen content in the arterial blood is down, while that in the venous blood is up. The arterial-venous oxygen difference is sharply reduced. During the tonic phase, the rate of oxygen uptake by the tissues of the cerebral hemispheres is depressed. Oxygen tension in the brain drops at the height of the seizure. Adaptation and acclimatization to hypoxia result in increased tolerance to an epileptogenic factor.

Neuhaus, G. Adaptation to chronic oxygen deficiency: physiological findings in morbus caeruleus. Jahrbuch der Wissenschaftlichen Gesellschaft für Luftfahrt (Braunschweig), pp. 213-221 (1954). A comparative investigation of adaptation mechanisms in chronic hypoxia was conducted with fully compensated morbus caeruleus patients and altitude-acclimatized, healthy subjects. Under similar altitude conditions, equated for arterial oxygen tension, the patients exhibited superior performance and higher resistance to acute anoxia. Physiological differences were basically due to increased arterial CO_2 tension in the presence of an alveolar tension comparable to that of altitude-acclimatized subjects. Oxygen deficiency is a factor in the production of polycythemia and pseudovascularization. The importance of venous oxygen tension is seen in the correlation between effects of anoxia on the organism and the venous oxygen tension, regardless whether anoxia is produced by primary venous or primary arterial hypoxia. These findings are discussed in relation to phylogenetic adaptation mechanisms and cellular research.

Nevison, T.O., et al. 1960-1961 Himalayan scientific and mountaineering expedition. I. USAF high-altitude physiological studies. Presented at Scientific Program of Thirty-Third Annual Aerospace Medical Association Meeting, Atlantic City, N.J., 9-12 April, 1962. The United States Air Force participated in a Himalayan expedition led by Sir Edmund Hillary. The study of mechanisms of acclimatization and effects of prolonged exposure to altitude was a major objective. A physiological laboratory was established at 19,000 feet. Eight physiologists spent periods up to five months at this altitude or higher. This paper presents results of total body water determinations and respiratory, EKG, EEG recordings made during exercise and rest at altitudes up to 24, 500 feet.

Newman, M. T. Biological adaptation of man to his environment heat, cold, altitude and nutrition. Ann. Ny. Acad. Sci. 91(3):617-633 (1961). It seems clear, at least in general outline, that the nature and degree of human adaptations to facets of the environment, unrelated in a direct sense to disease, may indeed reflect upon reactions to disease situations. There are many hints of this fuller relationship between man's adaptation to his climatic and nutritional environments and his reactions to disease that promise rich scientific dividends.

Newsom, B. D., and D. J. Kimeldorf. Increased tolerance to hypoxia in irradiated and in food-deprived rats. Naval Radiolcgical Defense Lab., AD 25352, San Francisco, Calif. (6 Aug. 1953). The survival rates for groups of rats exposed to lethal levels of hypoxia in an altitude-simulating chamber were determined at various intervals after X-irradiation. Irradiated rats were significantly more resistant to the lethal effects of hypoxia than non-irradiated controls; this effect disappears approximately five days following 500 or 600 r of total body irradiation. Since the increase in tolerance occurred during the post-irradiation anorectic period, a study was made to determine the effects

of food deprivation upon the hypoxic tolerance of non-irradiated animals. When deprived of food for 72 hours, nonirradiated animals exhibited an increase in hypoxic tolerance comparable to that of irradiated animals. A similar change in tolerance after irradiation was noted when the duration of survival time under conditions of asphyxiation was used as the test criterion. The increased tolerance of irradiated rats to the above conditions appears to be, at least in part, a consequence of post-irradiation anorexia.

Newton, J. L. The assessment of maximal oxygen intake. J. Sports Med. Physical Fitness: 164-169 (1963).

Nichols, J. Quantitative histochemical changes in the adrenal following exposure to anoxia. J. Association Med. 19:171 (1948).

Nielsen, M., and H. Smith. Studies on the regulation of respiration in acute hypoxia. Acta Physiol. Scand. 24:292-313 (1951).

Nienweller, H., and K. E. Schaefer. Development of hyaline membranes and atelectasis in experimental chronic respiratory acidosis. Proc. Soc. Exp. Biol. Med. 110:804 (1962).

Noell, W. K., and A. E. Kornmuller. Effect of oxygen deficiency on cortex; bioelectrical study. Pfluger. Arch. Ges. Physiol. 247:685-712 (1944).

Nordea, I., and L. Lundholm. The effects of acidosis and alkalosis on resistance of mice to hypoxia. Acta Pharmacol. (Kobenhavn) 19(4):356-364 (1962). Mice were subjected to acute progressive hypoxia and lethal oxygen tension was determined. At the same time, the oxygen consumption was recorded at different partial pressures of oxygen. Subcutaneous injection of hydrochloric acid substantially increased the animals resistance to hypoxia in acute experiments; concurrently, they tolerated a greater reduction in their oxygen consumption than did control animals. Administration of sodium bicarbonate reduced the resistance to hypoxia; these animals had a higher oxygen consumption than the controls at correspondingly low oxygen partial pressures.

O

Oettli, T. Acclimatization difficulties in the pper Engadine. Practitioner 180 (1079):590-595 (May 1958).

Ohwaki, Y. Influence of low atmospheric pressure on discriminative reaction time. Tohoku Psychol. Folia (Sendai, Japan) 15(3-4):45-53 (1957). While exposed to simulated altitudes of 3500 and 5000 meters, five subjects performed a discriminative reaction-time task at normal barometric pressure. Under normal pressure, the reaction times were three times longer for stimuli alternated irregularly than for a regular pattern. At low atmospheric pressure, the discriminative reaction times were lengthened considerably under both conditions. The extent of deterioration varied greatly according to the individual.

Olson, R.E. "Excess lactate" and anaerobiosis. Ann. Intern. Med. 59:960-963 (1963).

Opitz, E. and J. Saathoff. Survival of primary gasping center in various mammalian species before and after acclimatization to high altitude. Arch. Ges. Physiol. 255:485-491 (1952).

Opitz, E. Increased vascularization of tissue due to acclimatization to high altitude: significance for oxygen transport. Exper. Med. Surg. 9:389-403 (May-Nov. 1951).

Opitz, E. Increase in respiratory volume produced by oxygen deficiency in persons adapted to high altitudes. Ver.. Deutch. Ges.. J. Kreislaufforch pp. 86-92 (1940).

Oprisescu, S. Biochemical changes in organism produced by altitude. Rev. San. Mil., (Bucharest) 35:1248-1253 (Nov. 1936).

Ordonez, J. H. Duration of QT intervals: study of 400 electrocardiograms of normal persons adapted to altitude of 2640 meters An. Soc. Biol. (Bogota) 1:53-59 (Mar. 1943).

Ordonez, J.H. Melanosis of unknown origin: nutritional deficiency, life at high altitude, and pituitary disorders as possible causes. An. Soc. Biol. (Bogota) 2:121-146 (July 1946).

Ormea, F. Research on the threshold of tactile skin sensitivity at high altitudes. Dermatologica (Basel) 121:377-386 (Dec. 1960).

Ormea, F. Research on the threshold of sensitivity to skin pain at high altitudes Dermatologica (Basel) 121:371-377 (Dec. 1960).

Otis, A. B., and G. S. Husson. Physiological adaptation to chronic hypoxia: D. Oxygen. John Hopkins Univ. School of Med., AD 107-958, Baltimore, Md. Some features of oxygen transport in hypoxia of circulatory origin are presented and compared with altitude hypoxia. The polycythemia which develops in both types of hypoxia is described and discussed. It is concluded that polycythemia is an adaptation of a special advantage in hypoxia of circulatory origin.

Otis, A. B., H. Rahn, A. Epstein, and W. O. Fenn. Performance as related to composition of alveolar air. Amer. J. Physiol. 146:207-221 (1946).

Otis, A. B.. and W. C. Bembower. Effect of density on resistance to respiratory gas flow in man. J. Appl. Physiol. 2:300-306 (1949-1950). The alveolar pressures required to produce various velocities of respiratory gas flow have been measured in 20 human subjects breathing air and 80-percent helium - 20-percent oxygen. In 3 subjects a similar comparison has been made between air breathing at ground level and at simulated altitudes of 18,000 and 36,000 feet. Less alveolar pressure is required to produce a given velocity of flow when a person breathes 80-percent helium - 20-percent oxygen at ground level or air at altitude than when he breathes air at ground level; this effect may

be due to a decreased turbulence in the less dense gases. The data also suggest that some parts of the respiratory tract may dilate when one breathes at high velocities.

Oudat, J. Physiologic and clinical observations in high mountains Presse Med. 59:297-300 (7 Mar. 1951).

Oudat, J. Effect of oxygen inhalation in high mountains Presse Med. 59:326-327 (7 Mar. 1951).

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Pace, N., et al. The increase in hypoxia tolerance of normal men accompanying the polycythemia induced by transfusion of erythrocytes. Amer. J. Physiol. 148:152-163 (1947).

Pace, N. U., B. Bezer, and B. E. Vaughn. Erythrolysis on return of altitude acclimatized individuals to sea level. J. Appl. Physiol. (2): 141-144 (Sept. 1956). Observations were made of the red blood cell and hemoglobin levels of ten sea-level residents before, during, and after an 11-week sojourn at altitudes above 10,000 feet. It was found that the polycythemia required 6 to 7 weeks to reach stabilization, while red cell and hemoglobin levels were reduced to one-third of the stabilized altitude within 17 days after descent to sea-level condition. Comparison of the normal rate of disappearance of red blood cells with the observed rate indicated that both a decrease in the rate of erythropoiesis and an increase in the rate of erythrolysis were necessary to account for the rapid restoration of the polycythemic blood cell counts to a normal value.

Palma, O. A. Human life at high altitudes. Prensa Med. Argent. 24:500-503 (10 Mar. 1937).

Paribok, V. P. Effect of acclimatization to hypoxia on the radiosensitivity of the nuclear structures of animals. Tsitologia 3:602-5 (Sept. - Oct. 1961).

Pashaer, T. G. Acid-base equilibrium and glutathione in blood of persons performing exercise of short duration in high altitude. Med. Z. 7:69-73 (1937).

Pauli, H. G. Contributions to the problem of respiratory regulation during altitude acclimatization. Pfluger. Arch Ges. Physiol. 278:447-466 (1964.) Respiratory regulation was studied in 18 subjects during residence at an altitude of 1,780 feet and during visits of 2 to 25 days at 11,340 feet. Values for respiratory minute volume during air breathing and the reduction in minute volume with 40- to 60-percent oxygen breathing were both elevated during exposure to altitude. Arterial hemoglobin concentration was increased at altitude, arterial oxygen saturation was generally decreased, and blood carbon dioxide tension was decreased. The respiratory response to arterial acid-base changes was slightly reduced at altitude. No significant change

was observed in the buffering capacity of the blood. Cerebrospinal fluid acid-base values remained at more stable level than arterial value at altitude.

Pawal, N.E., R.T. Clark, and H.I. Chinn. Changes in brain blood volume during acclimatization to high altitude. School of Aviation Med., AD35376, Randolph AFB, Texas. The brain blood volume of rats increased by 11.7 percent during acclimatization to 18,000 feet. The systemic blood volume during the same period increased by 31 percent. The length, number, and diameter of the capillary bed was tripled after acclimatization The discrepancy between brain and systemic blood increase during acclimatization is discussed.

Payne, I.R. Effect of altitude and diet on hematopoiesis and serum cholesterol. J. Nutrit. 64(3):433-446 (10 Mar. 1958). This study was instigated to obtain biochemical and physical data on women residing at an altitude of 7200 feet and in a geographic area different from that of California (at sea level) where a similar study was made. It was felt that data gathered by the same method in both studies would provide good comparative information to determine if altitude and geographical conditions have any effect on serum-cholesterol levels.

Pena, F.S. Ocular lesions due to sun at high altitude. Arch. Oftal. (B. Air.) 26:237-240 (May 1951).

Penaloza, D., et al. The influence of high altitude on the electrical activity of the heart: Electrocardiographic and vectorcardiographic observations in newborn, infants, and children. School of Aviation Med., Report 60-79, Aerospace Med. Center, Brooks AFB, Texas. Five hundred and forty normal children were studied, 350 at sea level and 190 in Morococha, Peru (14,900 feet above sea level). The comparative study was made in children of five age groups, ranging from newborn to 14 years. The electrocardiographic and vectorcardiographic characteristics of the healthy children living permanently at high altitudes are not comparable with those of the normal children at sea level. Therefore, a high altitude environment is an important source of electrocardiographic and vectorcardiographic variability in healthy children.

Penaloza, D., M. Echevarria, E. Marticorena, and R. Gamboa. Early cardiographic changes produced by ascending to high altitudes. Amer. Heart J. 56(4):493-500 (Oct. 1958). Electrocardiographic observations were made on subjects taken from sea level to high altitude, where they remained from 16 to 30 days. The first changes were observed a few

hours after arrival at high altitude, and modifications were evident some days later. The changes disappeared 1 to 2 weeks after the subjects returned to sea level. The following changes were observed: Variations of the AP vector—probably related to wandering pacemaker in the sinus node; changes of the QRS complex—explained by variations in the cardiac position; and modifications of the venticular recovery process—probably related to subacute overloading of the right ventricle and to right ventricular ischemia as a consequence of the modifications of the pulmonary circulation in an environment of anoxic anoxia.

Penaloza, D. Electrocardiograph changes observed during the first month of residence at high altitude. Air Force School of Aviation Med., Report No. 58-79:1-8 Randolph AFB, Texas (Aug. 1958).

Penaloza, D., and M. Echevarria. Electrocardiographic observations on ten subjects at sea level and during one year residence at high altitudes. Amer. Heart J. 54(6):811-822 (Dec. 1957). Ten male subjects between the ages of 18 and 23 were taken from Lima, Peru (sea level), to Morococha (altitude of 14,900 feet). Electrocardiographic changes which occurred during one year of residence in Morococha were studied. No variations of the auricular activation process were observed.

Observations made in the ventricular activation process indicate variations in cardiac position, and an incipient development of right ventricular hypertrophy. Studies of the ventricular repolarization process revealed early response to anoxemia and right ventricular overloading. Comparisons with the electrocardiographs of some of the Morocochan natives show that one year of residence at high altitude was not sufficient for complete cardiac acclimatization.

Penaloza, D., et al. The influence of high altitudes on the electrical activity of the heart. Electrocardiographic and vectorcardiographic observations in adolescence and adulthood. SAM-TDR-62-87, Aug. 1962.

Penaloza, D., et al. Pulmonary hypertension in healthy men born and living at high altitudes. Amer. J. Cardiol. 1(2):150-157 (1963). Right heart catheterization studies were performed in 38 healthy men 17 to 34 years of age born and living at high altitudes. In order to obtain comparative data, a similar investigation was made in 25 healthy men born and living at sea level. Mild preliminary hypertension and a moderate increase of the pulmonary vascular resistance and right ventricular work were found in men living permanently at high altitudes. Pulmonary wedge pressure, cardiac output and heart rate did not show significant difference from the data obtained at sea level. The changes occurring in the heart and pulmonary circulation in men living permanently at high altitude are not quite comparable with those changes described in temporary residents at high altitudes, nor with those experimentally obtained by acute hypoxia. The augmented pulmonary vascular resistance in the high-altitude dweller is related to the anatomic changes in the small pulmonary arteries and arterioles which have been described by other investigators. Functional factors such as vasoconstriction, hypervolemia and polycythemia do not play an important role in the mechanism of the pulmonary hypertension at high altitudes. The role of the pulmonary hypertension in the complex mechanism of acclimatization to life at high altitude is not well understood. Apparently pulmonary hypertension would not accomplish a useful part in this mechanism. If is possible, however, that pulmonary hypertension, in association with other factors such as hyperventilation and an extensive capillary bed of the lungs, plays a role in improving the arterial oxygenation in men living at high altitudes.

Pena Matias, L. A. Human serum proteins; filter paper electrophoresis; Normal values at sea level (Lima) and at altitude (Morococha). Comparison with chemical fractionation: method of Wolfson, Cohen, Calvay, and Ichiva. An. Fac. Med. (Lima) 39(2):512-542 (1956). Comparative analysis of blood protein by means of filter paper electrophoresis in normal persons living near sea level at Lima, Peru, (150 meters) and at Morococha, Peru, (4540 meters) demonstrated certain differences in the levels of albumin and gamma globulin. No significant difference was observed in proteinemia, values for total blood proteins, or alpha and beta globulins between the subjects at sea level and at altitude. Blood protein values for the two groups obtained by means of Wolfson, Cohen, Calvay and Ichiva s chemical fractionation method generally agreed with those obtained by electrophoresis.

Penman, R. W. B., and H. D. Lingh. Changes in ventilatory response to hypoxia after breathing CO_2 mixtures. Presented at the Mill Hill Meeting of the Physiological Society, 3-4 Nov. 1961. During the course of an investigation into the relationship between alveolar CO_2 tension and ventilatory responses to hypoxia, it was noted that the response to hypoxia was much reduced in the first hour after a period of breathing CO_2 in air mixtures. It was felt that a further examination of this problem might throw some light on the apparent contradictions in the results of Astrom (1953), and Cormack, Cunningham, and Gee (1957).

Perazzo, D. L. Altitude and urinary 17-ketosteroids. Sem. Med. (B. Air.) 109(12):60-64 (12 July 1956). An increase was found in the urinary excretion of 17-ketosteroids of four subjects decompressed at the rate of 500 meters per minute to a simulated altitude of 4000 meters. At 2000 meters, ketosteroid excretion was relatively insignificant in 50 percent of the subjects. Only under the effect of marked hypoxia (breathing of 12.7-percent oxygen mixture, corresponding to 4000 meters of altitude) was there evidence of an increase in the urinary 17-ketosteroid level in two subjects; it remained unchanged in the other subjects.

Perdriel, G. Tolerance of precorneal lenses to altitude. Bull. Soc. Med. Milit. Franc. 52(3):82-85 (Mar. 1958).

Peres, G. Effects of altitude on the magnesium content of rat tissues. J. Physiol. (Paris) 54:392-3 (Mar.-Apr. 1962).

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Peterson, E. W., B. S. Kent, and H. R. Ripley. Intestinal gas volume at altitude. Canad. Med. Assoc. 50:523-526 (June 1944). The investigations illustrate the fact that gas filled abdominal viscera expand at altitude. Up to 10,000 feet, this expansion is not very great; only 1.5 times the original volume. This expansion follows the principle of Boyles' Law and is not resisted to any extent by the abdominal parietis.

Peterson, E. W. Cerebrospinal fluid pressure: critical review. Arch. Neurol. Psychiat. 52:400-408 (Nov. 1944).

Petit, J. M., G. Milic-Emili, and J. Troquet. Maximum mechanical exertion of the thorax and altitude. Rev. Med. Aero. (Paris) 2:273-6 (May-June 1963).

Petit, J. M., G. Milic-Emili, and J. Troquet. Pulmonary dynamic exertion and altitude. Rev. Med. Aero. (Paris) 2:276-9 (May-June 1963).

Petty, L., W. Bartlett, and J. L. Chapin. Effects of altitude, acidosis, and alkalosis upon hypoxic threshold. Proc. Soc. Exp. Biol. Med. 90(3):664-666 Dec. 1955. The hypoxic threshold, (pressure at which ventilation began to increase during breathing of 50 percent O_2 in N_2) was found to be 179 mm. Hg tracheal O_2 pressure in subjects acclimatized to an altitude of 14,150 feet and 128 mm. in subjects living at sea level. Subjects acclimatized to 5300 feet ingested 6 gm. of

NH_4Cl/day for 5 days prior to the experiment (acidosis) which increased the threshold to 164 mm. while the ingestion of 15 to 30 gm. $NaHCO_3$/day for 5 days (alkalosis) decreased the threshold to 107 mm. NH_4Cl could be expected to counteract the effects of altitude on alveolar O_2 tension and pH; the threshold, however, changed in the direction of increased altitude. These factors were discounted as threshold determinants. It is suggested that the threshold is determined by the CO_2 at the bicarbonate level to which the subject is acclimatized.

Petrun, N.M. The role of respiration through the skin in compensating difficult or disturbed pulmonary gas exchange in man. AFSC N65-17781, Foreign Technology Div., Wright-Patterson AFB, Ohio. In order to investigate the influence of elevated oxygen concentrations in the air surrounding the skin on the rate at which it penetrates the skin and on the extent of pulmonary gas exchange, the entire body of each test subject, except the head, was enclosed in a lightweight diving suit. Results showed that absorption of oxygen through the surface of the skin increased by 33 times, while the amount of carbon dioxide excreted was 45 percent smaller. Also, there was a marked decline in absorption of oxygen by the lungs of test subjects. This was 25 percent smaller after 30 minutes of the experiment and had dropped to

31 percent after an hour. Cutaneous respiration, it was concluded, is capable of compensating for inadequacies of pulmonary gas exchange.

Phillips, L. W., R. L. Griswold, and N. Pace. Cognitive changes at high altitude. Physiol. Report 13(2):423-430 (Oct. 1963). The effects of hypoxia on cognitive functions were investigated with two types of problem solving and two immediate memory tasks. The first experiment, carried out with five subjects for 3 days at 12,470-feet altitude after prior practice at sea level, showed no changes in performance. In the second experiment, practice effects were counterbalanced with seven subjects spending two days at sea level and two days at 14,250-feet altitude. Performance was significantly impaired in one type of problem-solving task and improved in the other. There were no significant changes in immediate memory. The improvement in problem-solving was significantly correlated with changes in temperature and pulse rate, but the improvement was not significantly related to these measures. Peformance under hypoxic conditions may depend upon an interaction among several factors including the degree of practice, complexity of the psychological functions, and the subject's ability to respond to awareness of physiological deficits by increased efforts.

Pichotka, J., O. Creutzfeldt, and W. Höfler. The changes of body temperature and oxygen uptake during alteration between normal and lowered oxygen tensions. Naunyn-Schmiedeberg Arch. Path. 225(4):323-334 (1955). Experiments were conducted with guinea pigs to examine the shifts in oxygen uptake and the rectal temperature during transfer from normal oxygen tension to lowered oxygen tension (80-percent O_2), and return to normal oxygen tension. Reduction of the oxygen tension led to extreme fall in the oxygen uptake which then rose gradually to a plateau within 50 to 100 minutes. A return to normal oxygen tension at first doubled the oxygen uptake which then receded to normal values. These shifts in oxygen uptake occurred simultaneously with changes in the tactical temperature. The increase of oxygen uptake during lowered oxygen tension is accompanied by a fall in the rectal temperature which stabilizes at a constant value at the same time as the oxygen uptake. A return to normal oxygen tension reverses this behavior. The shifts in oxygen uptake regardless of oxygen tension are seen as part of a regulatory mechanism.

Pickett, A.P., and E.J. Van Liere. The effect of anoxia on gastric secretions from Pavlov and Heidenhain pouch dogs. Amer. J. Physiol. 4:637-641 (Nov. 1939). There were differences in the two groups in the response to anoxia: the pH did not change in the Pavlov group until

a partial pressure of oxygen of 63 mm. Hg was reached, but the Heidenhain group was affected at a less severe degree of anoxia (80 mm. Hg). The data obtained from total acids are exactly the reverse of the data obtained from pH. Total chlorides in the Pavlov group were not affected by the degrees of anoxia used in this test, but were decreased in the Heidenhain group as early as at a partial pressure of oxygen of 94 mm. Hg. In general, then, the Heidenhain group is affected by less severe degrees of anoxia than the Pavlov group.

Pickford, M. Respiratory adaptation. Lancet 2:1225-1226 (11 Dec. 1954).

Picon-Reategui, E. Basal metabolic rate, body composition, and creatinine excretion at high altitudes. School of Aviation Med. Rept. No. 58-97:1-10 Randolph AFB, Texas (Nov. 1958). BMR, creatinine excretion, and body composition were determined in 17 healthy adult males living in Morococha, Peru (altitude 14,900 feet). The results seem to justify the following conclusions: using body surface as a standard of reference and following the criterion of Boothby et al., the BMR of high-altitude residents had the same range as that of healthy adults at sea level. When predicted values are based on the formula of Harris and Benedict, the BMR is higher in the high-altitude resident. However, when ideal weight is substituted for actual weight in this formula, the results agree with the standards of Boothby et al. The coefficients of correlation calculated with the data obtained show that the lean body mass or its components are the best standards of reference to predict the BMR. Among the body fluids, total body water proved to be the best standard of reference. Of course, lean body mass is just 0.73 of total body water. The higher oxygen consumption per kilogram of lean body mass, cell mass, or cell solids, found in high-altitude residents seems to be one of the many mechanisms developed by the body in its process of adaptation to low-oxygen tensions. Formulas have been developed to predict BMR from surface area and body composition and to predict body composition from BMR and creatinine excretion.

Picon-Reategui, E. Intravenous glucose tolerance test at sea level and at high altitude. School of Aviation Med. AD126-289, Randolph AFB Texas (Dec. 1956). Determinations of the capillary blood content of glucose, before and after the intravenous administration of glucose, were made in healthy men living at sea level and in native residents of Morococha, Peru (14,900 feet). The basal concentration of glucose in the blood was lower at high altitudes, but a higher value was observed in this environment four minutes after its administration. The drop in the blood glucose, after the initial rise, occurred more rapidly at high altitudes. No symptoms of hypoglycemia were observed among the natives of Morococha, in spite of the very low values of blood glucose observed. At sea level and at high altitudes, the utilization of glucose varied in direct relation to the concentration of this substance in the blood.

Picon-Reatigui, E. Studies on the metabolism of carbohydrates at sea level and at high altitude. School of Aviation Med. Report No. 56:107, Randolph AFB, Texas. Two groups of healthy adult males (one group living in Lima, Peru, at sea level; the other in Morococha at 14,900-feet altitude) were studied to learn the effect of altitude on the assimilation of glucose. The fasting venous blood values of glucose, pyruvic and lactic acids, inorganic phosphate and potassium, and the changes which occur after the oral administration of glucose were determined. The concentration of glucose in the venous and capillary blood samples was found to be consistently lower at high altitude. The extrahepatic assimilation of glucose was similar at the two elevations. There was no difference in the fasting concentration of lactic acid in venous blood and no significant differences in the basal concentrations of pyruvic acid and potassium and in changes which occur after ingestion of glucose. At high altitude there was a greater concentration of inorganic phosphate in the blood, but the trend of changes was the same in the two locations.

Picon-Reategui, E., R. Lozano, and J. Valdivieso. Body composition at sea level and high altitude. J. Appl. Physiol. 16(4):589-592 (1961). Simultaneous determinations of total body water and extracellular fluid, using the antipyrine and sucrose infusion methods, have been carried out in 28 adult male residents at sea level and in 28 residents at an altitude of 14, 900 feet. Body composition was calculated from these data. The various body spaces, expressed in percentage of body weight, were similar in the two groups with the exception of the extracellular fluid, which was greater in those in the high-altitude group ($P<0.01$). Neither racial characteristics nor altitude appear to be factors generally affecting body composition. In individuals having adequate caloric intake, body composition seems to be principally influenced by physical activity. In fact, physical inactivity appeared to produce a loss of active tissue and its replacement by fat.

Picon-Reategui, E. Basal metabolic rate and body composition at high altitudes. J. Appl. Physiol. 16(3):431-434 (1961). Basal metabolic rate (BMR) and body composition were determined in 17 healthy adult males living at an altitude of 14, 900 feet above sea level. Using body surface area as a standard of reference and following the criterion of Boothby, et al (Amer. J. Physiol. 116-468, 1963). The BMR of the high-altitude resident fell within the limits considered normal for healthy adults at sea level. A comparison with the data by investigators in the United States and in India shows that, when either fat free body mass (FFM) cell mass (C), or cell solids (S) are the standard of reference, the BMR is higher in the high-altitude resident. The higher O_2

consumption per kilogram of FFM, C, or S in the high altitude resident seems to be one of the many mechanisms developed by the body in its process of adaptation to low O_2 tension.

Picon-Reategui, E., G.R. Fryers, M.L. Berlin, and J.H. Lawrence. Effects of reducing the atmospheric pressure on body water content of rats. Amer. J. Physiol. 172(1):33-36 (1953). Groups of rats were exposed to a simulated altitude of 15,000 feet. The relative humidity in the decompression chamber was maintained at 60±5 percent and the temperature at 25±2 °C. Water was freely available in open dishes. Body water determinations were made using tritiated water as an isotopic diluent, and the animals were weighed prior to each determination. Control studies were carried out simultaneously on animals kept at sea level. Maximum reduction in weight was found to be reached after about 7 days of altitude exposure. Thereafter, a gradual restoration of body weight was observed, the animals nearly regaining their initial weight in about 30 days. The water deficiency reached its maximum after about five days of exposure, and recovery was slightly slower than that from the weight loss, still continuing after 30 days. A total of 14.4 cc. of water per 100 g. of body weight (or 20 percent of body water content) had been lost at the period of maximal water depletion.

Picon-Reategui, E. Cre .inine excretion and body composition at high altitudes. Air Force School of Aviation Med. Report No. 58-98; 1-8 Randolph AFB, Texas (Feb. 1959).

Piery, M., and J. Enselme. Reactions of acclimatization and of non-adaptation. Nature (London) 144:731-733 (29 Oct. 1939).

Piery, M., J. Enselme, and C. Peschiera. Experimental study of biologic effect of prolonged stay at high altitude; effect on blood gases and erythrocytes. C.R. Acad. Sci. 208:1254-1256 (17 April 1939).

Piery, M., J. Enselme, and C. Perschiera. Chemical adaptations in man to atmospheric depression at high altitude. J. Med. Lyon 20:409-419 (5 July 1939).

Piery, M., J. Enselme, and C. Peschiera. Experimental study of biologic influence of prolonged stay at high altitude; modifications of hepatic and muscular iron content. C.R. Acad. Sci. 208:1441-1442 (1 May 1939).

Piery, M., and M. Nulhand. Winter sports in mountains: reactions of organisms; adaptation and training; indications and counterindications. J. Med. Lyon 23:7-16 (5 Jun. 1942).

Plas, Labusse, Missenarad, and C. Goryon. Cardiovascular behavior in high altitude. Rev. Med. Aero. 10:275-298 (July-Sept. 1947).

Plas, F., and J. Bourdinand. Changes in the electrocardiogram following repeated flight in pressurised cabins (cabins with a constant pressure differential). Rev. Med. Aero. (Paris)8(1):5-10(1953). Periodic examinations of about 60 aviators exposed regularly to flights in pressurized cockpits revealed the following clinical symptoms: about one-third of the subjects complained of an increase in weight of about 4 kg. in three months, and 20 kg. within a year; the total lipid content of the blood increased from 5.2 to 9.04 g. per 1000 cc. the basal metabolism rate decreased by 5.3 percent. In addition, subjective symptoms such as a mental lassitude, affecting primarily the memory and the sense of judgement, and tiredness of the eye and ear were experienced. The only objective symptom noted in two cases were a transitory deficiency of the T-wave in the electrocardiogram. Speculation on the pathogenesis of this "adaptation syndrome" suggests further investigation of the individual hormone levels and water metabolism, and the effects of combustion gases in the plane of ultrasonic and atmospheric ionization.

Platts, M. M., and M. S. Graves. The composition of the blood in respiratory acidosis. Chem. Sci. 16:695 (1957).

Polonovski, M., G. Bog, and J. Cheymol. Altitude, anoxia, and ammoniuria. C.R. Soc. Biol. 134:414-416 (1940).

Popova, T. V. Interoceptive reflexes in dogs in hypoxemia. Biull. Eksp. Biol. Med. 39(6):32-36 (June 1955). Dogs inhaled mixtures containing 6 to 12 percent oxygen, which corresponded to an altitude of 4500 to 9500 meters. This treatment brought about two-phase interoceptive reflex changes at all hypoxemic conditions; a considerable increase in the reflex reaction during the first phase, followed by a weakening or complete suppression of reflect reaction in the second phase. The increase in the interoceptive reflexes during the first phase was accompanied by a fall in the stimulation threshold and by clearly defined pressor reflexes at the sub-threshold level of stimulation. The transition to the second phase, as shown by gasometric studies, was not connected with any substantial fall in the blood oxygen saturation. Return to atmospheric pressure normalized all interoceptive reflex manifestation. It was concluded that in acute and chronic hypoxia the principles which regulate the course of interoceptive reflex manifestations are essentially the same.

Porras, F.K. Total cholesterolemia and lipemia in workers at altitude, An. Fac. Med. (Lima) 45:231-260 (1962). Cholesterol, total lipid, protein, and hemoglobin content of the blood were determined for 100 laborers living at La Oroya (Peruvian Andes, 3,730 meters above sea level) to study possible effects of altitude acclimatization on these constituents. Nutritional deficiencies forced 72 subjects to be disregarded. The remaining 28 had average cholesterol values of 161 mg. 100 ml., lipids 573 mg., proteins 7.75 g., and hemoglobin 19.1 g. There was no demonstrable effect of altitude on cholesterol and lipids, while the protein and hemoglobin levels were changed in the manner already established by earlier workers. All values were influenced by nutrition much more than by altitude.

Posternak, J. Dark adaptation on Jungfraujoch. Helv. Physiol. Pharmacol. 6:516-523 (1948).

Pozdnyakova, R. Z. Influence of oxygen starvation on interceptive reflexes (femoral-artery chemoreceptors). AFSC N65-17786, Foreign Technology Div., Wright-Patterson AFB, Ohio. The excitability of the femoral-artery chemoreceptor was investigated under conditions of oxygen deficiency by the change during hypoxia in the interoceptive reflexes

Indicators observed were oxygen and carbon dioxide contents of the arterial blood and the pH. Experiments were made with dogs that had been anesthetized by intravenous injection of sodium thiopental. It was concluded that under the conditions of mild hypoxia and circulatory hypoxia, the interoceptive reflexes from the chemoreceptors of the peripheral vessels are intensified, caused by an increase in the excitability of the peripheral end of the interoceptive analyzer.

Prast, J.W., and W.K. Noell. Indication of earlier stages of human hypoxia by electroencephalometric means. J. Aviation Med. 19:426-434 (1948).

Prast, J.W. and W.K. Noell. Anoxia warning device: The slow wave activity of the brain during earlier stages of oxygen leak. AF School of Aviation. Med. Project No. 21-02-050, Report No. 1, Randolph AFB, Texas (Mar. 1949).

Prentice, T. C., and E. A. Mirand. Effect of low-oxygen duration and liver damage on plasma erythropoietin titer in hypoxic animals. Exp. Med. and Surg. 15(2-3):176-180 (1957). Normal rats placed in a low oxygen atmosphere (10-percent oxygen) for periods ranging from 4 to 48 hours revealed definite elevation of plasma erythropoietin (EPF) titer up to 24 hours, as judged by Fe^{59} uptake assay using hypophysectomized rats. After 48 hours, the level returned to normal. Previous experiments demonstrated normal levels after five days in a hypoxic (10-percent oxygen) atmosphere. Therefore, there is a prompt rise in plasma EPF under the hypoxic stimulus, returning to normal in 48 hours and remaining there for up to 5 days. Severe liver damage associated with hypoxia tends to prolong the time during which EPF is elevated in hypoxic rats. Lesser degrees of liver damage do not produce similar results.

Primac, F. Ya. Hypoxidoses and autoallergy: Their importance in internal pathology. AFSC N65-17790, Foreign Technology Div., Wright-Patterson AFB, Ohio. Investigation of the gas composition of the blood in persons suffering from severe forms of endocarditis enables the identification of patients in whom the mounting manifestations of arterial hypoxemia are combined with signs of tissue hypoxia.

Disturbances to the vascular structure and function should be regarded as one of the essential signs of hypoxidosis and the autoallergia that accompanies it. Study of vascular tissue permeability in persons with manifest hypoxia and vascular dystonia indicated a considerable increase in the amount of fluid escaping from the vascular stream, as well as an increase in the albumin content. This circumstance is of essential importance both in the exacerbation of the manifestations of hypoxidosis, and in the development of subsequent autosensitization due to native proteins sweated from the vascular stream.

Prinzmetal, M. F., L. Lonergan, and S. Brill. Effects of anoxemia on intrapleural pressure in dogs. Proc. Soc. Exp. Biol. Med. 29:191 (1931).

Prokhorova, M. L., L. S. Romanova, and G. P. Sokolva. Rate of lipid and carbohydrate renewal in the brain and liver in hypoxia. AFSC N65-17814, Foreign Technology Div., Wright-Patterson AFB, Ohio. Hypoxia was induced in white rats by injection of sodium nitrite as the methemoglobin-forming agent. Content and rate of renewal of cerebral lipids and rate of cerebroside renewal were unchanged in hypoxia. The rate of ganglioside renewal from glucose

was almost halved. Total lipid and cholesterol contents of the liver decreased. The glycogen content of the brain decreased by 25 to 30 percent and by a factor of 4 in the liver. The rate of glycogen renewal was also sharply altered. The specific activity of the cerebral glycogen was reduced by a factor of 1.8 and hepatic glycogen by 2.6. The radioactivity of the cerebral glycogen per gram of tissue decreased by a factor of almost 11.

Puccio, V. Absolute orientation in space. Effect of moderate hypoxia on the evaluation of positions in space, reached by means of passive body displacement. Riv. Med. Aero. (Rome) 18(4):848-921 (Oct. - Dec. 1955). Blindfolded subjects (fastened to a movable stretcher and mounted on a double wheel) estimated their position in space (vertical and horizontal) after passive body displacements slow enough to avoid vestibular stimulation. The margin of error was significantly higher in the first estimations, decreasing with successive ones. Experiments were carried out at ground level and at 300- to 400-meters simulated altitude. Unacclimatized subjects in moderately anoxic condition displayed the following effects: a slightly increased margin of error, indicating moderate impairment of absolute orientation; difficulty in judging the degree of orientation; the need of uncertainty in the estimation. It is concluded that anoxia affects higher mental activity which in turn causes an instability in absolute orientation.

Pugh, L.G.C.E. Tolerance in a Nepalese pilgrim to extreme cold at altitude. J. Appl. Physiol. 18:1234-1238(Nov. 1963). Body temperature and respiratory experiments are reported on a Nepalese pilgrim who survived, uninjured, 4 days of exposure at 15,000 to 17,500 feet in midwinter, wearing only light clothing and no shoes or gloves. His resistance to cold depended on elevation of metabolism, and unlike tolerance of immersion in cold water, was not related to subcutaneous fat thickness. He slept soundly in spite of the cold and so did not become exhausted. In 3- to 4-hour experiments at 0°C (clothed), rectal temperature and skin temperature over the trunk showed only minor changes; hand and foot temperature did not fall below 10 to 13°C. Maintenance of body temperature was accounted for by elevation of metabolism.

Pugh, L.G.C.E. Blood volume and hemoglobin concentration at altitudes above 18,000 feet (5500 meters). J. Physiol. 170:344-354 (Mar. 1964). Blood volume, hematocrit, and hemoglobin concentration were followed in six subjects during prolonged acclimatization at varying altitudes up to 19,000 feet. After 18 weeks at heights ranging from

13,000 to 19,000 feet, blood volume was lower than at sea level in four out of six subjects, the mean reduction being 9 percent. During further periods of 3 to 6 weeks, and 9 to 14 weeks, at (or above) 19,000 feet, blood volume rose slowly, the final mean value being 9 percent above the sea level control value. The fall in blood volume was associated with a reduction in plasma volume which amounted to 27 percent. Plasma volume subsequently rose slowly, but the final mean value was still 19 percent below sea level control value. Red cell volume and total hemoglobin rose progressively, reaching mean values of 49 percent above the sea-level control value. Hemoglobin concentration rose by 30 percent in the first 18 weeks, and 8 percent during the following 9 to 14 weeks. According to data collected on eight expeditions to the Himalaya and Karakoram, hemoglobin concentrations in plainsmen living at 18,000 feet and above do not reach the values (22.9 g./100 ml.) reported in Andean natives living at 17,500 feet. The mean value for eight parties was 20.19 g./100 ml. It was concluded that change in plasma volume is a major factor in the regulation of hemoglobin concentration under these conditions.

Pugh, L.G.C.E. Muscular exercise at great altitudes. J. Appl. Physiol. 19(3):431-440 (May 1964). Oxygen intake, ventilation, and heart rate were measured in six subjects performing ergometer exercise at various altitudes from sea level to 7,440 meters (24,400 feet; barometric pressu 300 mm. Hg) during a Himalayan expedition lasting 8 months. Oxygen intake for a given work rate was constant and independent of altitude up to the maximum work rate that could be maintained for 5 minutes. Maximum oxygen intake declined with increase of altitude, reaching 1.46 liters per minute at 7,440 meters (24,400 feet) in the best subject. Ventilation (STPD) for a given work rate was independent of altitude in light and moderate exercise but increased at each altitude as maximum oxygen intake was approached. Ventilation values of 140 to 200 liters (BTPS) per minute were observed at altitudes above 4,650 meters (15,300 feet). Heart rates at altitude were higher at low and moderate work intensities, but the same as or lower than the corresponding sea level value for the same work load as maximum oxygen intake was approached. Breathing oxygen at sea level pressure at 5,800 meters (19,000 feet) reduced ventilation and heart rate for a given work rate, restored work capacity almost to sea level values, and increased maximum heart rate. With the aid of data on blood, lung diffusion, and cardiac output from comparison studies, the oxygen transport system was analyzed in three subjects, including a high altitude Sherpa; and evidence is put forward that lung

diffusion, cardiac output, and the high oxygen cost of extensive ventilation contributed to the limitation of exercise at 5,800 meters (19,000 feet).

Pugh, L.G.C.E. Physiological and medical aspects of the Himalayan Scientific and Mountaineering Expedition, 1960-1961. Brit. Med. J. 2,621 (1962).

Pugh, L.G.C.E. Hemoglobin levels on the British Himalayan expedition to Cho Oyer in 1952 and Everest in 1953. J. Physiol. (London) 126(2):38-39 (29 Nov. 1954).

Pugh, L.G.C.E. The effects of oxygen on acclimatized men at high altitude. Proc. Roy. Soc. 193(910):14-17 (15 Dec. 1954). Knowledge of the effects of oxygen on acclimatized men at altitudes above 22,000 feet depends entirely on the experience of mountaineers on Everest. Experimental data are, however, available up to 20,000 feet from work done on the Cho Oyer expedition in 1952, and up to 21,000 feet from work done on Everest the following year. The results of this experimental work are presented here, followed by the empirical findings of the Everest climbers in 1953.

Pugh, L. G. C. E. Cardiac output in muscular exercise at 5,800 meters (19,000 feet). J. Appl. Physiol. 19(3):441-447 (May 1964). Cardiac output during muscular exercise was estimated by the acetylene technique for four members of the Himalayan Scientific and Mountaineering Expedition of 1960-1961 at sea level and 5,800 meters (19,000 feet). The output for a given work intensity of 5,800 meters was comparable with the output for the same work intensity at sea level, but the maximum output was reduced, the mean value being 16 liters per minute, compared with 23 liters per minute at sea level. Heart rates during light and moderate exercise were higher than the rates observed for the same work intensity at sea level. The maximum heart rate during exercise was limited to 130 to 150 beats per minute compared with 180 to 196 beats per minute at sea level. The stroke volume at altitude was lower than at sea level pressure, and heart rate for a given work intensity was reduced, but the maximum heart rate increased. Indirect evidence suggested that maximum cardiac output increased, but probably not to the sea level values, because of the increased hemoglobin and lowered heart rate.

Pugh. L. G. C. E. Animals in high altitudes; man above 5,000 meters in mountain exploration. In Adaptation to environment, chapter 55, Washington, D.C.: Amer. Physiol. Soc., 1964.

Pugh, L. G. C. E. Resting ventilation and alveolar air on Mount Everest: with remarks on the relation of barometric pressure to altitude in mountains. J. Physiol. (London) 135:59 (1957).

Pugh, L. G. C. E. Muscular exercise on Mount Everest. J. Physiol. (London) 141(2):233-261 (30 Apr. 1958).

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Rabbeno, A. Influence of some climatic factors on cholesterine of blood and on suprarenal capsules: actions of rarefied air on cholesterine and fat in blood. Arch. Sci. Biol. 9:161-167 (Dec. 1926).

Rabbeno, A. Cholesterine of suprarenal capsule at high altitude. Arch. Sci. Biol. 9:168-177 (Dec. 1926).

Rahn, H., and A.B. Otis. Man's respiratory response during and after acclimatization to high altitudes. Amer. J. Physiol. 157:445-462 (1949). With the aid of an O_2-CO_2 diagram, data are presented which allow prediction of the alveolar oxygen and carbon dioxide composition as well as the related alveolar ventilation when man is exposed acutely to any altitude, during the process of respiratory acclimatization, and when acclimatization is complete. In addition, the alveolar pathways can be predicted and described once man acclimatized to any particular altitude is suddenly exposed to higher or lower oxygen pressures. These predictions are verified, in part, by an acclimatization study at an altitude of 9500 feet for a 3-week period. Evidence is presented for a pO_2 threshold of the chemoreceptor drive of ventilation at approximately 100 mm. Hg which has been observed in the ventilation curves of persons acclimatized to altitude. However, in acute exposures where the alveolar pO_2 is reduced to 50 to 60 mm. Hg, hyperventilation responses are completely inhibited for at least one hour. This inhibition is the result of the pH rise due to the decreased oxyhemoglobin saturation. If the alveolar pO_2 in acute exposure falls below 50 to 60 mm. Hg, immediate hyperventilation occurs. Exposures of more than one hour at 9500 feet result in a lowering of the pCO_2 exponentially with time; final levels are reached after 3 or 4 days. After respiratory acclimatizations to 9500 feet, the respiratory system becomes more sensitive to carbon dioxide. This response was tested by breathing various carbon dioxide mixtures and analyzing the alveolar air after breath holding. Data are presented which show the reduction of breath-holding time during acclimatization to various altitudes. The various findings emphasize that a large part of the respiratory acclimatization to high altitudes is an adaptation to a lowered carbon dioxide tension.

Rahn, H., H. T. Bahnson, J. F. Muxworthy, and J. M. Hagen. Adaptation to high altitude; changes in breath-holding time. J. Appl. Physiol. 6(3):154-157 (Sept. 1953) Changes in maximal breath-holding time after breathing air or oxygen as well as the alveolar gas concentrations were reported in 4 subjects during a 7-day exposure to an altitude of 14,100 feet (4300 meters). After initial exposure to this altitude, the breath-holding time tested with both air and oxygen was found to be gradually reduced over the next 5 to 7 days. Simultaneously, the carbon dioxide differences between the normal resting concentrations and that obtained at the breaking point were also reduced. These changes are interpreted as indicating an increased sensitivity of the respiratory system to carbon dioxide. The index of breath-holding time is suggested as a simple tool in evaluating respiratory adaptation to altitude.

Rahn, H., S.M.Lenney, and J.C.Mithoefu. Adaptations to high altitude; respiratory responses to CO_2 and O_2. J. Appl. Physiol. 6:3158-3162 (Sept. 1953). After a residence of 5 to 6 days on Mt. Evans, Colo. (14,100 feet), CO_2 breathing and breath-holding tests with oxygen were compared with those obtained 2 weeks previously at Rochester, N.Y. (550 feet). All subjects demonstrated an increased sensitivity to CO_2 after adaptation to altitude. Breath-holding studies were also carried out after breathing various O_2-N_2 gas mixtures. Under these conditions of acute respiratory acidosis, a definite oxygen threshold cannot be established; with adaptation to altitude the lack of a definite threshold persists. The analysis of these breath-holding tests, furthermore,

suggests that no change has taken place in the sensitivity of the respiratory system to oxygen.

Rahn, H., and W. A. Dale. Rate of gas absorption during atelectasis. Amer. J. Physiol. 170:606 (1952).

Ramalingaswami, V., and P.S.Venkatachalam. Hematologic studies on healthy adult men in Coanoar and Ootacamund (altitude 6000 and 7500 feet) Indian J. Med. Res. 38:17-28 (Jan. 1950).

Rasin, S. D. Changes in the basic nerve processes of dogs at lower atmospheric pressure. Med. Zh. (Kiev) 23(2):10-16 (1953). Disturbances in the higher nervous activity develop in dogs following short-duration exposure to reduced atmospheric pressure in pressure chambers or upon ascent to high altitudes on Mount Elbrus. Disturbances in the conditioned reflexes become manifest at air rarefaction equivalent to an altitude of 5000 meters. In one subject, disturbance in reflex activity disappeared with a 10-minute exposure to altitude; in another the disturbances disappeared only when the subject was brought down to an altitude of 1000 meters. Under conditions equivalent to a 7000-meter altitude, disturbances in the activity of conditioned reflexes were more pronounced. After a short exposure, two dogs began to show symptoms of diffuse inhibition, which lasted only a short time and gradually

disappeared with the descent to normal pressure. Under the influence of prolonged hypoxia and conditions of actual high-mountain altitudes, disturbances in the conditioned reflex activity of the dogs began to appear at considerably lower air rarefaction (2200 meters) and persisted for two days. At an actual mountain altitude of 4250 meters, the disturbances were of a profounder character and persisted throughout the entire period of sojourn on the mountain at that altitude. Following the descent to sea level, the disturbances in the conditioned reflex activity of three out of four dogs completely disappeared, pointing to the fact that the disturbances were due to hypoxia and not to any extraneous factor.

Ravenna, P. Modification of production of antibodies observed in healthy man during sojourn in high mountains. Minerva Med. 1:893-896 (16 June 1933).

Raverdino, G., and O. Stiglich. Vestibular excitation in low and high mountains in rest and after fatigue. Valsalva 16:208-213 (June 1940).

Redfield, A.C. Accommodation to anoxemia of high altitude. Boston Med. Sci. J. 187:841-844 (7 Dec. 1922).

Reed, D.J., and R.H. Kellogg. Effect of sleep on hypoxic stimulation of breathing at sea level and altitude. J. Appl. Physiol. 15(6):1130-1134 (1960). The effect of sleep on the level of hypoxia in four adult, male, sea-level residents was studied at sea level, during 23 days at 14,250 feet, and after return to sea level. The subjects, awake and asleep, breathed graded O_2-N_2 mixtures; each breathing period was followed by inhalation of high O_2 gas. Sleep did not significantly affect the hypoxic drive of breathing as evaluated from the steady-state levels of ventilation or from the immediate respiratory depression produced by interrupting hypoxia. At the ambient altitude O_2-tension, arterial O_2 saturation, indicated by ear oximeter, fell 4 to 8 percent with sleep. The fall in arterial oxygenation can probably explain the increased severity of mountain sickness which is commonly associated with sleep at altitude.

Reed, D.J., and R.H. Kellogg. Changes in respiratory response to CO_2 during natural sleep at sea level and at altitude. J. Appl. Physiol. 13(3):325-330 (Nov. 1958). The effect of natural sleep on the breathing of three adult, male, sea-level residents was studied at sea level, during a four-week sojourn at 14,250 feet, and after return to sea level. In each case the respiratory minute volume decreased by about 2l per minute during sleep. To investigate the role of altered responsiveness to CO_2 in sleep, graded CO_2 mixtures, containing sufficient O_2 to preclude hypoxia during the test, were administered to subjects while they were awake and asleep. At sea level, sleep shifted the curve relating respiratory minute volume to alveolar CO_2 tension (CO_2 response curve) to the right by 3 to 5 mm. Hg so that higher CO_2 tensions were required to simulate a given level of ventilation. In the tests at altitude, the waking CO_2 response curve was 10 to 12 mm. Hg to the left of its sea-level position. During sleep at altitude, the curve shifted to the right from the new position by 3 to 5 mm. Hg. This shift suggests that the effects of sleep were superimposed on the respiratory readjustment accompanying altitude acclimatization. During sleep at sea level or altitude, there was little if any change in the shape or slope of the CO_2 response curve.

Reeves, J.T., E.B. Grover, and R.F. Grover. Circulatory responses to high altitude in the cat and rabbit. J. Appl. Physiol. 18(3):575-579 (May 1963). Cats were taken from Denver (5200 feet) to Mount Evans (14,150 feet) with the anticipation that the degree of hypoxia would induce pulmonary hypertension. Rabbits were included for comparison with the cats. All cats died without developing pulmonary hypertension or right heart failure, in spite of arterial and mixed venous oxygen tensions maintained well above those of the rabbit. Presumably, the

cats' inability to survive was not a failure of oxygen transport to the arterial blood or to the systemic capillary. Paradoxically, five of eight rabbits survived despite poor arterial blood oxygenation. The rabbits developed marked polycythemia associated with modest right-ventricular hypertension and dilatation.

Reeves, J.L., E.B. Grover, and R.F. Grover. Pulmonary circulation and oxygen transport in lambs at high altitude. J. Appl. Physiol. 18(3):560-566 (May 1963). The oxygen transport and pulmonary hemodynamics of lambs native to low altitude were evaluated in Denver and on Mount Evans (12,700 feet). Because the hemoglobin-oxygen dissociation curve is placed well to the right of most other mammals, markedly depressed arterial oxygen saturation (59 percent) occurred at high altitude. However, the lambs adapted remarkably well and showed normal rapid growth. The mixed venous oxygen tension was relatively well maintained; primarily, by a narrowing of the arterio-venous oxygen gradient to 11 mm. Hg. Despite the marked hypoxemia, elevation of the pulmonary artery pressure was not a consistent finding and was neither marked nor sustained when it occurred.

Reeves, J.L. Influence of intermittent exposure to simulated altitude on plasma and tissue electrolytes in rats. AF School of Aviation Med.,

Report No. 61-37:1-20, Randolph AFB, Texas (Feb. 1961). Young adult rats exposed four hours each day for twenty-six to twenty-eight weeks to barometric pressure of 380 mm. Hg in an altitude chamber exhibited changes in body weight, organ weight, and hematocrit of the same order of magnitude as rats continuously exposed to the same conditions. Plasma cation concentration was not affected, but a substantial shift occurred in the relative concentrations of anions. With the exception of the ventricular myocardium, the electrolyte composition of soft tissues did not change materially. The femoral shaft, the most severely affected of the tissues, exhibited depletion of calcium, phosphorus, and sodium and, at the same time, an accumulation of potassium. The decrease of bone electrolytes was in a ratio which indicated complete solution of the apatite crystal rather than anionic or cationic exchange reactions.

Reichel, H. Cardiac death in the mountains from the viewpoint of a physiologist. Sportarzt (Koln) 13(3):65-67 (Mar. 1962). The effect of hypoxia on the cardiovascular system is reviewed from a practical standpoint. Even a relatively slight decrease in the oxygen saturation of the arterial blood at low altitudes (2000 to 2500 meters) may cause serious disturbances in the heart excitatory rhythm, due to hypoxia of the heart-chamber musculature in the case of coronary sclerosis, and

may result in ventricular fibrillation. In the presence of any minor symptoms of an existing coronary sclerosis (angina pains), especially in the case of individuals past forty years of age, the use of mountain highways or mountain passes should be prohibited.

Rein, H. Respiration in high altitude. Luftfahrt-Med. Abhandl. 1:23-29. (1936)

Reissmann, K.R., W.L. Burkhardt, and B. Hoelscher. Blood destruction in polycythemia induced by hypoxia. Blood 7(3):337-349 (1952). Hemoglobin catabolism before, during, and after exposure to a simulated altitude of 20,000 feet was studied in bile fistula dogs with references to developing and diminishing polycythemia. The life span of red cells was found to be the same in altitude-exposed animals as in controls kept at ground level, i.e., 115 days. Polycythemic blood levels returned to normal within about 6 to 8 weeks after return to ground level, as a result of depressed erythropoiesis combined with increased red blood cell destruction. The increase in red blood cells during altitude exposure was accompanied by a marked increase in bile pigment output.

Reissmann, K.R. Studies on the mechanism of erythropoietic stimulation in parabiotic rats during hypoxia. Blood 5:372-380 (1950).

Reissmann, K. R. Blood volume in the dog during altitude acclimatization. Amer. J. Physiol. 167:52-58 (Oct. 1951). Plasma, cell and blood volumes, and total circulatory hemoglobin were determined in a group of dogs before, during, and after acclimatization to a 20,000-foot altitude. During altitude exposure, the plasma volume decreased gradually to a constant level which was 75 percent of ground-level value. The cell volume reached a plateau of 170 percent of the ground level value in the fifth week of exposure and returned to normal within 6 weeks after discontinuance of exposure. The total circulatory hemoglobin paralleled the cell volume; and in some subjects increases of 200 gm. hemoglobin were observed during 5 weeks of exposure. The total blood volume remained almost constant in the first 2 weeks of exposure, then increased slowly and reached a plateau of 125 percent of the ground level value in the fifth week of exposure.

Reugger-Peilmann, L. Anthropometric and physiological (respiratory) observations in 30 inhabitants of Davos, Switzerland. Z. Ges. Aivat. 13:202-208 (30 May 1927).

Ressel, F. A. Contribution to the study of polycythemia at altitude. Rev. Clin. Esp. 62(4):239-251 (31 Aug. 1956). High altitude polycythemia, determined in men and women living in Pulacazo, Bolivia

(4250 meters) appears to reach lower values than those previously reported, and is characterized by an increase of about 500,000 erythrocytes (2.38-percent increase per 1000 meters of altitude). Hemoglobin values remain within normal limits. Tabulated average values are included for erythrocytes and hemoglobin in both sexes.

Rey de Castro, J.C., and B. Iglesias. Mechanisms of natural acclimatization: preliminary report on anatomic studies at high altitudes. AF School of Aviation Med., AD 126-831, Randolph AFB, Texas. This is a preliminary report on anatomic studies of pathologic specimens obtained from persons acclimatized to altitudes of about 4000 meters. The majority of the subjects had died in accidents. The organs investigated included the lungs, trachea, bronchi, heart, liver, spleen, kidney, striated muscles, sexual glands, and in a few cases, brain and suprarenal glands.

Reyes, R.J., and J.R. Neville. Cellular oxygen consumption at low oxygen tensions. Presented at the thirty-fourth Annual Meeting of the Aerospace Medical Association, Los Angeles, Calif., April-May 1963.

Reynafarje, B. Myoglobin content and enzymatic activity of human skeletal muscle—their relation with the process of adaptation to high altitude. SAM-TDR-62-89. Quantitative determinations of myoglobin were made

in the sartorius muscle of healthy human subjects, natives of sea-level and high-altitude areas. The specific activity of the reduced form of diphosphopyridine nucleotide oxidase (DPNH-oxidase), DPNH- and TPNH-cytochrome c reductases, transhydrogenase, and isocitric and lactic dehydrogenases were also examined. A significantly higher myoglobin concentration was found in the muscle of the high-altitude natives as compared with sea-level residents. The enzyme systems DPNH-oxidase, TPNH-cytochrome c reductase, and transhydrogenase similarly showed a significantly higher activity in altitude residents. It was concluded that the respiratory capacity of the muscle was apparently higher in natives living at high altitude than in those living at sea level. The enhanced enzymatic activity was probably related to the higher pigment content of the skeletal muscle. A discussion is included on the results on myoglobin determinations in several other muscles from certain sea-level patients.

Reynafarje, B. Pyridine nucleotide oxidases and transhydrogenase in acclimatization to high altitude. SAM-TDR-62-88, Nov. 1962. Activity of pyridine nucleotide, oxidases and transhydrogenase has been examined in heart, liver, and rectus femoris muscle of native sea-level and high-altitude guinea pigs. There was an enhanced, (reduced form) diphosphopyridine nucleotide oxidase (DPNH-oxidase)

and transhydrogenase activity in heart and muscle from animals adapted to high altitude. The higher activity in muscle at altitude was due solely to increase in ratio of red to white portions. Both groups showed the pigmented portion twice as active as the white one. In liver, neither the DPNH-oxidase system nor the transhydrogenase was significantly changed in their activity on a fresh-weight basis. Nevertheless, the DPNH-oxidase is higher at altitude wnen the activity is expressed per gram of nitrogen. The reduced form of triphosphopyridine nucleotide oxidase activity was not appreciably changed in any of the tissues. It was concluded that adaptation to high altitude is associated with apparent changes in the magnitude of the electron transport pathway. Increased activity in skeletal muscle is probably related to the tissue pigment content.

Reynafarje, B. Estudios de quimica tisular en la hipoxia. Presented at the Congreso Internacional de Ciencias Fisiologicas, Buenos Aires, 1959.

Reynafarje, C., and J. Ramos. Influence of altitude changes on intestinal iron absorption. J. Lab. Ciin. Med. 57(6):848-855 (June 1961). Intestinal iron absorption increased during the first day that 82 subjects were exposed to an altitude of 14,900 feet (Morococha, Peru) and

reached a maximum in one week and was less evident one month later. Iron absorption decreased in natives of altitude brought down to sea level (Lima, Peru), reached a minimum in 3 weeks, then increased to normal after 16 months. The absorption of iron was essentially the same in natives from high altitude as in sea-level subjects when each group was studied at its native locality. These findings suggest that a greater or smaller bone marrow demand, associated with changing red cell production, is the stimulus for the intestinal absorption of iron related to altitude changes rather than oxygen saturation of the blood or oxygen tension at the intestinal level.

Reynafarje, C., R. Lozano, and J. Val-Divieso. The polycythemia of high altitudes: iron metabolism and related aspects. Blood. 14(4):433-455 (Apr. 1959). An estimation of red blood cell formation in polycythemia of high altitude is of particular interest. It is well known that this type of polycythemia due to anoxic stimulus brought about by low-atmospheric pressure is reversible since it disappears when the subject returns to his normal barometric-pressure environment. A very close relationship exists between the degree of polycythemia and the altitude at which the permanent resident lives; in newcomers, the degree of response depends on the severity and the duration of the anoxic stimulus. A study of these problems is

presented chiefly on the basis of iron metabolism and also blood volume, the degree of reticulocytosis and the cytology of the bone marrow, as well as some aspects of hemoglobin pigment catabolism and red blood cell life span. Information has thus been obtained concerning the formation and the destruction of erythrocytes.

Reynafarje, C. Red cell life span in newborn at sea level and high altitude. Proc. Soc Exp. Biol. 100(2):256-258 (Feb. 1959). The life span of the red cells of groups of five newborn at high altitudes and at sea level was determined by "tagging" the cells with Cr^{51} and subsequently injecting them into healthy adults. The survival time of red cells in newborns is shorter than that observed in adult subjects. There was no appreciable difference in the results obtained in the new born at sea level and at high altitudes.

Reynafarje, C. Observations on the bone marrow of the newborn at high altitude. An. Fac. Med. (Lima) 42:618-629 (1959).

Reynafarje, C. The influence of high altitude on erythropoietic activity; homeostatic mechanisms. Presented at the Tenth Brookhaven Symposia in Biology, May 1958.

Reynafarje, C., and R. Lozano. Mechanisms of natural acclimatization: Observations of the iron metabolism and the free protoporphyrins of the erythrocytes in the polycythemia of high altitudes. AF School of Aviation Med., AD 119787, Randolph AFB, Texas (June 1956).

Observations on the iron metabolism, by means of the administration of Fe^{59}, and on the concentration of free protoporphyrins in the circulating red cells were made on four groups of subjects: men living at sea level, native residents at an altitude of 14,910 feet, men taken to high altitude for a temporary exposure, and subjects studied at sea level after their return from a six-month period of exposure to high altitudes. An increase of the erythropoietic activity which was observed in the group of residents at high altitude was even more accentuated during the first few days of exposure to the low-pressure environment. However, a depression of the erythropoietic activity was found on their return to sea level. An increase of the free erythro-protoporphyrins was found both in the men living permanently and in those dwelling temporarily at high altitude. The amount of this pigment tended to decrease in the men returning to sea level.

Reynafarje, C., A.J. Berlin, and J.H. Lawrence. Red cell life span in acclimatization. Proc. Soc. Exp. Biol. 87(1):101-102 (Oct. 1954).

Riesen, A.A., T.N. Tahmisian, and C.G. Mackenzie. Prolongation of consciousness in anoxia of high altitude by glucose. Proc. Soc. Exp. Biol. Med. 63:250-254 (Nov. 1946). The preflight administration of a single dose of glucose in water to individuals on a normal diet produced a significant increase in the resistance to unconsciousness from anoxia at 27,000 to 30,000 feet. The protection afforded flying personnel by the glucose solution was greater 30 to 50 minutes following its administration than after an interval of 60 to 80 minutes. At 27,000 feet, the mean duration of consciousness was increased by approximately 40 percent, or more than one minute, by the preflight ingestion of glucose solution. Vitamin C either alone or in conjunction with glucose, had no demonstrable effect on the duration of consciousness.

Riley, R.L., A.B. Otis, and C.S. Houston. Respiratory features of acclimatization to altitude, AF School of Aviation Med., AD49179, Randolph AFB, Texas. The following four phases of respiratory adjustment to altitude were observed in subjects during exposure to simulated altitudes up to 22,000 feet: (1) Period of lung washout - subjects exposed to 22,000 feet altitude for 30 minutes displayed a mean alveolar pCO_2 value of 25 mm., while the alveolar pO_2 value was 36 mm., effective ventilation was more than double the ground-level value. The exchange ratio of 1:2 indicated a 50 percent increase in CO_2 elimination. (2) Period of tissue washout - during a one-hour exposure to the same altitude, ventilation gradually decreased and at the same time the alveolar pCO_2 dropped. This behavior represented a compromise between the hypoxic stimulus and a hypocapnic inhibition. The alveolar exchange ratio fell until it almost reached a steady CO_2 exchange. Upon return to ground level, without the anoxic stimulus, ventilation was less in the first five minutes than the original ground level value. Tests carried out at 12, 000, 16, 000, 18, 000, and 20, 000 feet proved that higher altitudes induce greater ventilation, and the higher the initial use in alveolar exchange ratio, the greater the decrease in pCO_2. (3) Period of base exertion - during prolonged acclimatization to altitude, the blood buffer base (excess of fixed base over fixed acid in the blood) was reduced by selective excretion of fixed base and retention of fixed acid by the kidneys. (4) Regulation of tissue capillary pO_2 in acclimatization - the blood flow and hemoglobin concentration increased, raising the venous pO_2 and minimizing the drop of oxygen pressure between the arterial blood and the tissues.

Riley, R. L. Respiratory and circulatory changes during acclimatization to high altitude. Amer. J. Physiol. 149:565-588 (1947).

Riley, R. L., and C. S. Houston. Composition of alveolar air and volume of pulmonary ventilation during long exposure to high altitude. J. Appl. Physiol. 3:526-534 (Mar. 1951). Alveolar gas was sampled daily by the Haldane-Priestley method on 4 healthy subjects who were continuously exposed to gradually increasing simulated altitude in a low pressure chamber over a 35-day period. Ventilation was measured and arterial blood sampled on one of the four subjects each day. Ventilation BTPS increased steadily as altitude increased, though there were considerable individual differences. Total ventilation STPD and alveolar ventilation STPD remained approximately constant at increasing altitudes, alveolar pO_2 values corresponded closely to those found by Boothly in unacclimatized subjects; alveolar pCO_2 values were lower than Boothly's at the higher altitudes. The relationship between the alveolar values found in this study and those reported by Boothly can be explained by the differences in duration of exposures to simulated altitudes. The data are consistent with current concepts of the acclimatization process as presented by Rahn and Otis and with the concept of ventilatory control presented by Bjurstedt.

Rimiras, P.S., R. Hill, A.A. Krum, and A.W. Lis. Carbohydrate metabolism in fed and fasted rats exposed to an altitude of 12,470 feet. Amer. J. Physiol. 193(2):415-424 (May 1958). Blood sugar levels and the glycogen content of liver, heart, skeletal muscle, diaphragm, and kidney of both fed and fasted sea-level control rats were compared with those of fed and fasted rats (P) born at sea level and then exposed to an altitude of 12,470 feet for various periods of time, and with those of fed rats of the second filial generation (F_2) born and maintained at altitude. In the P animals after short-term (twenty-four and seventy-two hour) exposure, liver, heart, muscle, and diaphragm glycogen was markedly decreased in the fed animals as compared with the fed sea-level controls, and markedly increased in the fasted hypoxic animals as compared with the fasted sea-level controls. After long-term exposure of fed P animals, liver, heart, muscle, and diaphragm glycogen was the same as in fed controls after two and six months at altitude, and became markedly lower than in the controls after 10 months. In the F_2 rats, liver and muscle glycogen was markedly decreased when compared with the controls; in contrast, cardiac glycogen content was significantly higher in F_2 rats than in the controls. Changes were not observed in kidney glycogen. Hyperglycemia was observed in all P rats after twenty-four hours, and hypoglycemia after seventy-two hours at altitude. In the long-term experiments, glycemia was the same in experimental (P and F_2) and controls rats.

Ringenbach, G. Altitude polycythemia: Investigations in aviation medicine and at the Alpine station on Jungfraujoch. Sang. (Paris) 24:45-51 (1953).

Ringenbach, G. Question of existence of polyglobulism at high altitude: studies on Jungfrau at altitude of 3500 meters. J. Med. (Bordeaux) 129:248-251 (Mar. 1952).

Rivolier, J. Medicine and Mountain. In Medicine et Montagne, pp. 3-201. Paris: B. Arlhaud, 1956. This is a semi-scientific handbook on the medical and physiological problems associated with mountain expeditions and also provides practical recommendations for mountain climbers. An explanation of the various physical phenomena of high altitude and discussions of the physiology of respiration, muscular work, regulation of heat and cold, and acclimatization are included. Survival at high altitude is considered in terms of nutrition, oxygen supply, adequate training, equipment, and drugs. The symptoms, prevention, and treatment of altitude sickness, fatigue, sunburn, eye disorders, and injuries are also described.

Rivolier, J. Possibilities of physiological experimentation in the high mountains. Concours Med. (Paris) 76(52):4861-4862 (Dec. 1954). In order to study the physiological aspects of acclimatization to altitude, 10 subjects lived for two weeks on Mount Blanc (approximately 4000 meters). Cardiovascular function test, respiratory function tests (spirometric ventilation studies at rest and during effort, and alveolar air measurements), and oximetry were performed throughout

the experiment. The climatic, technical, and psychological problems encountered are discussed. The author notes that this type of physiological study away from the laboratory is of no value unless carefully and strictly executed.

Rivolier, J. The relation of cold and altitude to nutrition. Ann. Nutr. (Paris) 9(3):135-177 (1955). A general discussion is presented of questions of nutrition during extended exposures to cold and altitude. Subjects include the effects of cold on the basal metabolism, nutritional utilization hydration, time of gastric evacuation, problems of thermal loss, fatigue and digestive disturbances, and the physiological effects of altitude. Man's requirements for specific nutritional components are discussed, including minerals, vitamins, carbohydrates, fats, proteins, and caloric content. The nutritional requirements of airmen are briefly considered.

Rivolier, J. On acclimatization to altitude. Concours Med. (Paris) 77(18):1811-1818 (Apr. 1955). A general discussion is presented on the process of altitude acclimatization and the various protective measures used with ascent to high altitudes. The manifestations of mountain sickness (including headache, asthenia, lassitude, and fatigue), and digestive, nervous, and mental disorders, are noted as they occurred in mountain climbers of the French expedition to Makulu (8470 meters) in 1954.

Rivolier, J. Un futur centre de recherches a 6800 metres. Concours Med. (Paris) 80(36):3867-3868 (6 Sept. 1958).

Robocheit-Robbins, F.S., and G.H. Whipple. Hemoglobin production increase with severity of anemia. Amer. J. Physiol 2:263 (Sept. 1941).

Rodbard Simon. Effect of pulmonary venous pressure on nitrogen washout in the lung of the dog. Abstract in Circulation 26(4^2):792-793 (1962).

Roger, H. Life at high altitude. Presse Med. 47:1521-1524. (Nov. 1939)

Rogue, F.T. Influence of altitude and external temperature on blood pressure. J. Phillip. Med. Assoc. 19:677-682 (Nov. 1939).

Rojas, Soto, and C. Marquez. Some features of pulmonary insufficiency at high altitudes. Amer. Rev. Resp. Dis. 85(1):25-29 (Jan. 1962). The results are tabulated for pulmonary function tests (spirometer, blood gas analyses, mixed venous and arterial carbon dioxide, acid-base balance, hematocrit, and aveolar and arterial oxygen tension) performed in 65 patients with chronic pulmonary insufficiency and in normal subjects from the city of Puebla on the Mexican plateau (7080 feet).

Romano, J. Syncopal reactions during simulated exposure to high altitude in the decompression chamber. War Med. 4;475-489 (Nov. 1943)

Ross, J.M., H.M. Fairchild, J. Weldy, and A.C. Guyton. Autoregulation of blood by oxygen lack. Amer. J. Physiol. 202(1):21-24 (Jan. 1962). The effect of hemoglobin-oxygen saturation upon blood flow through the hind leg of the dog was studied by perfusing the femoral arteries of 5 normal and 9 spinal animals with blood in which the O_2 saturation varied between 100-0 percent and 100-10 percent, respectively. Blood was obtained from the lower lobe of the left lung as the lung was respired with a mixture of nitrogen and oxygen. By varying the ratio of the mixture, the blood oxygen saturation could be controlled exactly. Decreasing the oxygen saturation stepwise caused a correlated increase in blood flow through the leg. The results show that blood flow in the non-spinal dogs increased to an average of 3.4 times the normal value as oxygen saturation fell from 100 to 0 percent. In the spinal dogs, blood flow increased to an average of 3.1 times normal as O_2 saturation fell from 100 to 10 percent. These experiments demonstrate that the local tissues can autoregulate their blood flow to maintain an adequate supply of oxygen.

Rossen, R., E. Simonson, J. Baker, and J. Eckin. Patterns of the electroencephalogram during tilt, hypoxia and hypercapnia: response characteristics for normal aging subject. Abstract in Neurology 13(4):362 (1963).

Rossier, P.H. Studies on respiration and sickness at high altitudes and in respiratory regulation. Helvet. Med. Acta. 10:729-735 (Dec. 1943)

Rotta, A., and A. Lopez. The electrocardiogram at high altitudes. Rev. Peruana Cardiol. 6(3):167-181 (Sept.-Dec. 1957). From 120 electrocardiograms of normal adults, native or long-term residents of Morecocha, Peru, (4540 meters), twenty-three (19.2 percent) presented definite characteristic signs of right ventricular hypertrophy, thirty-nine (32.5 percent) showed highly suggestive signs of right ventricular hypertrophy, thirty-seven (30.8 percent) were classified as right bundle branch block, and twenty-one (17.5 percent) were found to be within normal limits. In most cases, regardless of the dominant pattern, a predominance of negative deflections of QRS complexes was observed in standard and precordial leads. These findings give the electrocardiogram at altitude a special characteristic not usually found at sea level and confirm the anatomic and radiographic finding of

right ventricular hypertrophy, previously obtained in individuals at altitude, which may be related to pulmonary hypertension usually found in man at altitude.

Rotta, A., et al. Pulmonary circulation at sea level and at high altitudes. J. Appl. Physiol. 9(3):328-336 (Mar. 1956). A comparative study was made of the pulmonary circulation of sea-level one-year, and native-born residents of high altitude environment (14,900 feet) and in two cases of chronic mountain sickness. Men living at high altitudes were characterized by hyperventilation, polycythemia and increased blood volume which were especially marked in cases of mountain sickness, decreased peripheral blood pressure (particularly systolic), increases in pulmonary vascular resistance and right ventricular work, and increases in pulmonary artery and right ventricle pressure which were most apparent in cases of mountain sickness and least apparent in temporary residents. No change was observed in pulse rate, and cardiac output was increased only in cases of mountain sickness. As a result of a greater hyperventilation in the temporary group, arterial blood hemoglobin oxygen saturation was decreased to a lesser extent in short-term residents than in native residents. Administration of 35-percent oxygen to high-altitude residents decreased pulse rate and cardiac output, but decreased pulmonary artery pressures only in cases of mountain sickness. Factors suggested to explain the rise in pulmonary pressure in high altitude residents include the increase in pulmonary vascular resistance produced by anoxia, changes in blood volume, hyperventilation, and low alveolar carbon dioxide.

Rotta, A. The cardio-thoracic index in the inhabitant of high altitudes. An. Fac. Med. (Lima) 38(1):17-21 (1955). The cardio-thoracic index showed an increase in persons living at Morococha, Peru (4540 meters). These subjects exhibited an increase in the transverse diameter of the heart and thorax in comparison with subjects living at Lima, Peru (143 meters). These findings indicate that physiological hemodynamic requirements induce the mechanism of adaptation to the low barometric pressure of high altitudes.

Rotta, A. Weight of the heart in normal man at altitude. Rev. Peruana Cardiol. 4(2):11-77 (July - Dec. 1955). Five hearts from natives of Morococha, Peru, (14,900 feet) who died suddenly in work accidents were dissected and the ventricular weights recorded. The left-to-right ventricle ratio showed gross right ventricular hypertrophy in two cases, moderate hypertrophy in another two, and a normal appearance in the remaining case. Calculation of Müller's function

index roughly followed the results of the left-to-right ventricle ratio. Pulmonary hypertension found in persons at high altitude is suggested as an etiological factor of right ventricular hypertrophy.

Rotta, A., A. Miranda, and J. Acosta. Cardiac dimensions at high altitudes: studies in adult males, in children and in athetes. Rev. Peruana Cardiol. 1:95-115 (Apr.-June 1952).

Rotta, A. Right heart catheterization at high altitudes. Presented at: Symposium Internacional Sobre Biologia de Altitud, Lima, Peru, 1949.

Rotta, A. Physiologic condition of heart in natives of high altitude. Amer. Heart J. 33:669-676 (May 1947). Measurements of cardiac size have been verified and a study has been made of some aspects of the circulatory physiology in native subjects living at 4540 meters above sea level. The determinations include the following: the study of 400 frontal X-ray films in which the transverse diameter and the frontal area of the cardiac silhouette were measured, using the method of Ungerleider and Gubuer; eighty fluoroscopic examinations of the heart, especially in the anterior oblique position; analysis of 100 electrocardiograms obtained in the 3 classic leads, 6 unipolar precordial leads, and 3 unipolar limb leads; and finally the study in

16 subjects of cardiac output per minute, stroke volume, arterial pressure, venous pressure, and arm-tongue and arm-lung circulation time.

Rotta, A., and J. Ascenzo. Graphic registration of heart sounds of natives. An. Fac. Med. (Lima) 26:147-160 (1944).

Rotta, A. Measurements of heart at sea level and at high altitudes. Gac. Med. (Lima) 1:44, (Oct. 1944).

Rotter, W. Effect of increased thyroid function on altitude tolerance; experimental study on animals. Arch. Kreislanfforsch. 9:226-257 (Oct. 1941).

Roughton, F. J. W. Respiratory functions of blood. AF School of Aviation Med., AD 49 179, Randolph AFB, Texas. The literature (74 references) on the following principles of respiratory physiology is reviewed in great detail: the partial pressure of dissolved O_2 and CO_2 in blood and the physiological importance of pO_2 and pCO_2; the transport of O_2 by the blood (significance of normal oxyhemoglobin dissociation curve, relation between Fe content, molecular weight, O_2 capacity, etc.); the speed of O_2 uptake by the blood in the lung;

the transport of CO_2 by the blood (rate of O_2 and CO_2 uptake by red cell suspensions); the diffusing capacity of the lung (calculation of average pO_2 gradient between alveolar air and blood in lung capillaries); nomographic representation of the relationship between O_2 and CO_2 and other substances in blood during the respiratory cycle at rest at sea level, and the effect of short exposure to low O_2 pressure. The nomogram of the blood of Chilean miners (residing at 17,600 feet and working at 19,000 feet) gives the following results: the total hemoglobin and hematocrit values show a 50-percent increase over sea-level values; while the oxyhemoglobin ratio is only a few percent higher, the total O_2 value carried by the blood is one-fifth greater than the O_2 in arterial blood at sea level when breathing air; the pH of the blood is normal; the lowered CO_2 is accompanied by a proportionate fall in the bicarbonate, thus compensating the respiratory alkalosis to low pO_2 in the acclimatized man.

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Circulation 27 (6):1094-1100 (1963). At altitudes of 13,250 to 14,900 feet in the Peruvian Andes, the "aortic" type of pulmonary trunk of the newborn is retained up to 9 years. This elastic configuration evokes into the "persistent" type which is observed for the remaining years of life. However, conversion of the "persistent" type into the "adult" type can be observed after 60 years of age. In places located between 11,300 to 12,600 feet of altitude, the "aortic" configuration of the pulmonary trunk is maintained up to 3 years. Cases with the "transitional" configuration can be observed at earlier ages, but apparently they rapidly evolve into the "persistent" type. The elastic configuration is observed principally in childhood and adolescence and also in a great proportion of young adults. By 55 years, (approximately), the totality of cases have developed into "adult" types. High altitude pulmonary hypertension present from birth, without doubt, is the result of the pathways of evolution of the elastic structure of the pulmonary trunk.

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excretion of 17-ketosteroids and reducing corticosteriods in healthy adult men living at sea level and in native residents living at an altitude of 14,900 feet. No significant differences were observed between the two groups, and the same degree of variability was observed at both altitudes.

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Scano, A. Determination of principal respiratory and cardiocirculatory responses to barometric depressions in groups of pilots. Rev. Med. Aero. (Rome) 21(3):455-460 (July-Sept. 1958). Data were recorded in ninety-six healthy jet pilots at sea level, at 3000 (526 mm. Hg pressure), and at 5500 meters altitude (379 mm. Hg pressure) for heart rate, respiratory rate, pulmonary and alveolar ventilation, alveolar gas tension, humeral blood pressure, and electrocardiogram. After arranging the subjects in homogeneous groups, experiments were conducted by standard methods. Collected values could then easily be used as calibration data for the evaluation of functional responses to low barometric pressures. Mean statistical values are reported together with group standard and individual deviations obtained from subjects who were repeatedly submitted to the experiment during different periods and under various conditions. A certain degree of acclimatization to altitude was noted in the subjects.

Scano, A., G. Muneri, F. Rossanigo, and B. Lagliamonte. Behavior of some respiratory value in man at barometric pressures of 760, 526, and 379 mm. Hg. Rev. Med. Aero. (Rome) 19(4):595-605 (Oct.-Dec. 1956). Respiratory studies were made in thirty-five normal jet pilots (average age, 25 years) at sea level and following decompression to simulated altitudes of 3000 and 5500 meters. There was no increase in respiratory frequency, an insignificant increase in pulmonary ventilation (2.2 percent) at 3000 meters, a significant increase (23.4 percent) at 5500 meters, and a relatively higher increase in alveolar ventilation. Alveolar carbon dioxide and oxygen tensions and respiratory quotient, when plotted on an oxygen-carbon dioxide diagram, resulted in a curve placed between the curve for non-acclimatized and acclimatized subjects. At the different altitudes, a correlation of 46.8 percent was found between the values for alveolar ventilation and alveolar carbon dioxide tension. The importance of respiratory variations is stressed for the careful and exact evaluation of the functional responses to barometric decompression.

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Semenov, Uy. V. On the influence of acute hypoxia in changing the acid resistance of erythrocytes of the growing organism. AFSC N65-17761, Foreign Technology Div., Wright-Patterson AFB, Ohio. Moderate or acute hypoxia was induced in young and mature dogs either by placing them in a pressure chamber in which the amount of ambient oxygen was regulated, or by a stricture of the trachea. Erythrograms were determined by the optical density of a blood sample hemolyzed in a 0.004 N HCl solution. In mature dogs, hypoxia caused an increase in the number of erythrocytes in the circulating blood, with a consistent increase in their fragility. In young dogs, hypoxia had no effect on the total number and the degree of fragility of the red blood cells.

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Seredenko, M. M. On certain peculiarities of the reaction of the organism to acute hypoxia. AFSC N65-17763, Foreign Technology Div., Wright-Patterson AFB, Ohio. In aged albino rats and dogs subjected to oxygen deficiency in a low pressure chamber at various altitudes, the degree of adaptation to hypoxia was lower than in mature animals. Ataxia, involuntary micturition, and defecation were noted at lower altitudes in the aged animals than in mature animals. The recovery time of respiratory rate and volume and of the pulse rate was increased. The character of the electrocardiogram was changed. In the aged animals, the physiological compensation of hypoxia, which consisted of an increase in pulmonary ventilation and oxygen uptake, did not produce an adequate oxygen saturation in the circulating blood sufficient for a rapid elimination of the oxygen debt.

Severinghaus, J. W., R. A. Mitchell, B. Richardson, and M. M. Singer. Respiratory control at high altitude suggesting active transport regulation of CSF pH. J. Appl. Physiol. 18:1155 (1963). The role of CSF pH and HCO_3 ion in stimulating respiration was studied in four men during acclimatization from sea level to 3800 meters for 8 days. CSF mean values for sea-level control, second, and eighth day at altitude were 7.388 and 7.336 and for arterial blood 7.474, 7.485, and 7.484 respectively. While subjects breathed high oxygen to

eliminate peripheral chemoreceptor drive, ventilatory response to four levels of alveolar CO_2 was determined, and for each value of P_ACO_2, arterial and CSF pH were computed. At altitude, the displacement of the ventilation response curves from the sea-level curves was: -10 mm. Hg P_ACO_2 + 0.06 pH unit for arterial blood, but -0.01 pH unit for CSF. CSF HCO_3 was 4 to 5 milliequivalents per liter lower than control within one to two days at altitude, whereas renal buffer base excretion only reduced blood standard bicarbonate 1 milliequivalent per liter after a week. CSF chloride and lactate rose about 6 and 1 milliequivalents per liter respectively. Thus, medullary respiratory chemoreceptor drive, initially reduced at altitude by hyperventilation alkalosis, is restored to normal during acclimatization by reduction in CSF HCO_3, the incremental ventilatory drive being supplied by peripheral chemoreceptors. The blood-CSF barrier appears to respond to the initial hyperventilation alkalosis by actively reducing CSF HCO_3; the data suggest that CSF pH is thus regulated by active transport of the blood—CSF barrier.

Severinghaus, J. W., R. A. Mitchell, B. Richardson, and M. M. Singer. CSF pH in man during acclimatization to high altitudes. Presented at forty-seventh Annual Meeting of the Federation of American Societies for Experimental Biology. CSF pH measurements in 4 men during the first 8 days at 3800 meters suggest that the gradual rise in ventilation, which occurred before renal reduction of blood buffer base, is due to reduction of CSF HCO_3 by active transport. Lumbar CSF pH was 7.328 at sea level and 7.338 (second day) and 7.336 (eighth day), while arterial pH was 7.424, 7.485 and 7.484. At altitude (eighth day) when P_IO_2 was increased to 190 for 19 minutes, P_ACO_2 rose 1.6 mm. Hg to 30.8, blood pH fell to 7.47, CSF pH fell to 7.32 (calculated from P_ACO_2). On the eigth day, the arterial pH and the CO_2 response curves (with P_AO_2 = 190) were shifted to +0.06 and -10 mm. Hg respectively, but CSF pH response curve (computed from P_ACO_2) was constant. On the second day, CSF $[HCO_3]$ fell 4.3 mM. while blood buffer base excretion reduced standard HCO_3 only 1 mM. after one week. Ten lifetime residents of Oroya, Peru (3730 meters) had CSF pH 7.327, HCO_3 21.5 mM., PCO_2 43.2 with arterial pH 7.431, and P_ACO_2 33.4. Six men at Morococha (4545 meters) and four at Licho (4820 meters) differed only in that P_{CO_2} was 0.5 and 1.5 mm. Hg lower, pH being constant. It is suggested that the cells which secrete CSF may regulate CSF $[H^+]$ and respond to the initial mild alkalosis of acute hypoxic by reducing CSF $[H_{CO_3}]$. The medullary respiratory chemoreceptor, also regulating CSF, then is stimulated by a lower P_{CO_2}.

Severinghaus, J. W. The role of the cerebrospinal fluid in human acclimatization to high altitude. Presented at forty-fourth Annual Session of the American College of Physicians, 1963.

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Shik, L. L. Oxygen starvation and the mechanisms compensating it in congenital heart defects of the blue and pallid types. AFSC N65-17789, Foreign Technology Div., Wright Patterson AFB, Ohio. Results obtained in a study of patients with blue-type defects are compared with the changes that take place in the physiological functions in hypoxic hypoxia, particularly during prolonged residence in the mountains. In patients with blue defects and in healthy individuals in the mountains, hyperventilation is caused by lowered oxygen partial pressure in the alveolar air and is governed by reflex intensification of breathing, produced by stimulation of chemoreceptors in the sino-carotic regions. In the mountains, hyperventilation represents an adaptive reaction to lower the extent of arterial hypoxemia. In patients with defects, the compensatory significance of hyperventilation

represents an adaptive reaction to lower the extent of arterial hypoxemia. In patients with defects, the compensatory significance of hyperventilation consists in prevention of hypercapnia although not lessening the extent of hypoxemia. In pallid cardiac defects, the basic compensatory reactions are directed toward preservation of an adequate blood supply to organs and tissues.

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Shumitskaya, N. M. Comparative physiological features of hematogenetic function in animals under the conditions of the high mountain climate. AFSC N65-17756. Foreign Technology Div., Wright-Patterson AFB, Ohio. Animals on different levels of evolution showed varying degrees of adaptation to high altitudes. Under conditions of oxygen deficiency, man exhibited greater deviations from normal values in blood composition and particularly in red blood count. At 4200-meter altitude, the number of erythrocytes in young adults increased by 4 percent. A definite shift to the left was noted. The presence of reticulocytes in the peripheral blood indicated an increase in hematopoietic activity.

Siebens, A. A., R. E. Smith, and C. F. Store. Effect of hypoxia on pulmonary vessels in man. Amer. J. Physiol. 180(2):428-432 (Feb. 1955). Pulmonary artery pressures and cardiac outputs of five patients were measured under "steady-state" conditions at rest and at exercise during anoxia and hypoxia. In each patient, exercise at the higher level of oxyhemoglobin saturation was associated with a small rise in pulmonary pressure and a fall in pulmonary vascular resistance. During hypoxia, a level of exercise which produced no

further augmentation of oxygen consumption or flow resulted in an additional rise in pressure and, consequently, an increase in resistance. This response was interpreted to indicate constriction of pulmonary vessels.

Siedlanowska, E. Arterial hypertension in the mountain climate. Pol. Tyg. Lek. 12(24):915-919 (10 June 1957). In an examination of 1212 persons between 20 and 88 years of age living in a mountain village 800 to 900 meters above sea level, hypertension was found more frequently in younger persons at this altitude than in those living in low-altitude villages. The incidence of discomfort and symptoms gradually increased with age and after 60 years of age it appeared more frequently in the mountain climate. Hypertension also appeared more frequently in women.

Sime, F., et al. Pulmonary hypertension in children born and living at high altitudes. Amer. J. Cardiol. 11(2):143-149 (Feb. 1963). Thirty-two healthy children aged 1 to 14 years, born and living at Morococha, Peru (14,900 feet) and Cerro de Pasco, Peru (14,200 feet), were studied by means of right heart catheterization. Mild pulmonary hypertension and increased pulmonary vascular resistance were found. Values of cardiac output and pulmonary wedge pressure were similar to sea-level values. Increased pulmonary vascular resistance was ascribed to structural changes in the small pulmonary arteries and arterioles. Pulmonary hypertension was greater in children than in adults (high altitudes), and greater in children under 5 years of age than in those 6 to 14. In the young group, pulmonary pressures were similar to those of newborn at sea level, which signifies that at high altitudes, in contrast with sea level, there is a delay in the evolution of pulmonary pressures with aging. The slow evolution agrees with the regression of right ventricular hypertrophy at high altitudes as demonstrated by anatomic, electrocardiographic, and vectorcardiographic studies. Pulmonary hypertension can be considered a form of primary pulmonary hypertension. The role of pulmonary hypertension in the high incidence of patent ductus arteriosus at high altitude is discussed.

Simonetti, C. Diametric values of heart of natives of Eritrean Plateaus. Boll. Soc. Ital. Med. Trop. 6:295-300 (1946).

Simonetti, C. Form and diametry of heart of native residents of Eritrean Plateaus. Boll. Soc. Ital. Med. Trop. 1(4):181-188 (1944).

Singer, R. B., and A. B. Hastings. An improved clinical method for the estimation of disturbances of the acid-base balance of human blood. Medicine 27:223 (1948).

Siri, W. Bolivian high altitude laboratory. J. Aviation Med. 29(8): 616-618 (Aug. 1958).

Siri, W. E., C. Reynafaye, N. I. Berline, and J. H. Lawrence. Body water at sea level and at altitude. J. Appl. Physiol. 7(3):333-334 (Nov. 1954). Total body water and body fat were determined in two groups of young, normal subjects: one group living at sea level, the other acclimated to 16,000 feet. The mean values for the two groups were normal for their age range and occupation. Thus, no evidence can be gained from this study to elucidate the changes in body water and body fat during and after acclimatization to low oxygen tension. Further studies on acclimatization will be carried out.

Sirotinin, N. N. Comparative physiology of acclimatization to the climate of the high mountains. AFSC N65-17732, Foreign Technology Div., Wright-Patterson AFB, Ohio. The human organism is sensitive to atmospheric oxygen deficiency, but possesses a mechanism of adaptation which begins to function at the early stages of hypoxia. Early compensation for oxygen deficiency brings about an increase in

pulmonary ventilation and blood circulation. The erythrocytes discharged from the reservoirs into the active circulation have a tendency to degenerate faster than the normal cells. Products of their disintegration act as stimuli for an increase in the hematopoiesis. The red cell count and the hemoglobin concentration rise gradually with a simultaneous normalization of pulmonary ventilation and blood flow rate. The increase in the total erythrocyte oxygenating surface area results in a certain shift of tissue mechanisms.

Slonim, A. D. Regulation of gas exchange in hypoxemia. In Makarchenko, A. F. (ed.). Oxygen Deficiency, pp. 190-195. Kiev: Akademiia Nauk, Ukrainekoi, 1964. Experimental results and observations on animals and man during the period of adaptation to atmospheric oxygen deficiency did not reveal a definite mechanism for the process of adaptation. The tissue gas exchange was either affected or remained unchanged. As a rule, hypoxia of short duration either increased or decreased the gas exchange. However, prolonged exposure to hypoxia resulted in normal oxygen uptake. Low temperatures, associated with high altitude, could play a role in the hypoxia effect. A depression of the thermoregulatory tonus of the skeletal muscles was usually observed during hypoxia and may be considered as one of the factors.

Smith, E.E., and J.W. Crowell. Influence of hematocrit ratio on survival of unacclimatized dogs at simulated high altitude. Amer. J. Physiol. 205:1172-1174 (Dec. 1963). Dogs with various hematocrit ratios were obtained by natural selection, hemorrhage, transfusion, and pretreatment with phenylhydrazine. Fifty-one dogs were placed in a closed chamber, and a 40,000 foot altitude was simulated and maintained for six hours. Most dogs with hematocrits less than 24 or greater than 66 died before the simulated altitude was attained; those with hematocrits of 24 to 30 survived from 1/2 to 5 hours. All dogs with hematocrits from 37 to 54 survived. With a group of 38 dogs, the same procedure was repeated at a simulated altitude of 50,000 feet. The survival group was composed of dogs with hematocrits from 36 to 46. Dogs with hematocrits from 40 to 41 remained conscious and active, whereas those with hematocrits on either side of this value became comatose. This experiment indicates that the optimum hematocrit ratio for survival of the unacclimatized dog at acutely induced high altitude is about 40. Deaths occurring on both sides of the optimum value may be explained by a simultaneous consideration of the curves depicting oxygen-carrying capacity of the blood and blood viscosity at all ranges of hematocrit.

Smith, H. P., A. E. Belt, H. R. Arnold, and J. B. Carrier. Blood volume changes at high altitudes. Amer. J. Physiol. 71:395-412 (Jan. 1925).

Smith, P. Studies in the chemistry of stress: I. The excretion of ether soluble metabolites in anoxia. AD 81809. Two series of chromatograms of extracts from acid-hydrolyzed urine sample of subjects exposed to a normal working day and mild anoxic conditions were compared to determine whether anoxia caused the appearance in urine of any abnormal metabolities. The samples were obtained from 5 apparently healthy young male subjects who were placed for 2-hour periods without oxygen in a decompression chamber at an altitude equivalent to 14,000 feet. Urine was collected just before descent. Urine from the control subjects was collected at about the same time during similar periods of normal activity. Chromatograms of not more than two of the five subjects' samples showed occasional abnormal spots. No over-all increase or decrease in anoxia was noted in the numbers and intensity of the total spots which were detected.

Smith, P. Studies in the chemistry of stress: III. Excretion in normal and anoxic subjects of substances absorbed by charcoal: AD 84372. Charcoal-absorbed material from the urine of normal and anoxic

subjects was chromatographed in ethanol-ammonia and butanol-acetic acid. An increase in the number of spots and a distribution shift from weak to stronger spots were observed in chromatograms from anoxic subjects. It is concluded that anoxia causes a general increase in the excretion of substances which can be detected by the charcoal absorption method.

Smith, P. Studies on the chemistry of stress: a new method of urine analysis: its application to the study of anoxia. AD 84 373. Material obtained by precipitation with ferric chloride from the urine of normal and anoxic subjects was chromatographed in ethanol-water-concentrated ammonia and butanol-acetic-acid water. An increase in number of spots was observed in chromatograms from anoxic subjects. The uncertainty of chemical transfer mechanisms in the preparation of the chromatographed material makes the method unsatisfactory for the quantitative analysis of urine.

Smith, W.W., W.S.Cool, F.Smith, and P.D. Altland. Effect of altitude-induced polycythemia and reticulocytosis on tolerance of rats to radiation. Amer. J. Physiol. 170(2):396-400 (1952). Rats exposed four hours a day for five weeks to a simulated altitude of 18,000 feet were irradiated with a single X-ray dose of 525, 625, and 760r. The mortality rate of altitude-acclimatized rats and ground controls was the same after the dose of 525r. After 625 and 760r, the mortality among altitude-acclimatized rats was greater than among ground controls. When altitude exposure was discontinued at the time of irradiation, the higher mortality rate persisted. Before irradiation, the number of circulating reticulocytes in the altitude-acclimatized subjects was two to three times that of the ground controls. Following irradiation, the number of circulating reticulocytes dropped to near zero in all groups, but increased 10 and 15 days after irradiation to 525 and 625r respectively, with higher rate increase in the altitude-acclimatized group. Reduction in hematocrit value was almost the same in altitude-acclimatized groups and ground controls. Altitude exposure showed no effects on leukocyte count or body weight. Contrary to expectations, experiments have shown that altitude-induced erythrocytic hyperplasia results in weakened tolerance to radiation.

Smolichev, E. P. On the effect of high mountain conditions on the protein content of the human blood. Biull, Eksp. Biol. Med. 50:78-82 (Oct. 1960).

Sofia, F., and B. Cearanino. Hemotologic study in native and European inhabitants of Eritrean plateaus: behavior of leukocytes. Boll. Soc. Ital. Med. Trop. 7:269-275 (1947).

Sofia, F., and E. Ciaranino. Hemotologic study in native and European inhabitants of Eritrean plateaus: behavior of erythrocytes and hemoglobin. Boll. Soc. Ital. Med. Trop. 7:262-268 (1947).

Solis, J. L. Volume of circulating plasma and blood in high altitude and their variations in relation to muscular exercise and time spent in high altitude. Arch. Latin. Amer. Med. Cardiol. Hemat. 6:241-264 (Sept.-Oct. 1936).

Soma, L., and M. Penna. Role of chemoreceptors in increasing cardiac output during acute anoxemia. Fed. Proc. 21(2):137 (1962).

Somogyi, J. C., H. Wiry, and F. Veryou. Changes in total volume of blood and plasma in high mountain regions. Helvet. Med. Acta (Supp. 6) 7:49-50 (1941).

Sorge, E. Acid-base equilibrium on Eritrean highlands studied in normal Europeans and Eritrean natives. Boll. Soc. Ital. Med. Trop. 1(2):66-70 (1943).

Soricelli, F. Acid-base equilibrium following roentgenotherapy on Eritrean plateau. Arch. Radiol. 21:142-148 (Nov. 1947).

Sorinson, S. N. The disruption of carbon dioxide interchange in chronic hypoxia, its pathogenesis and modes of treatments. AFSC N65-17800, Foreign Technology Div., Wright Patterson AFB, Ohio. This report gives an analysis of the disruptions of carbon dioxide interchange which occurs in chronic hypoxia of pulmonary etiology, based on the results of examination of patients with pneumosclerosis involving second and third degree respiratory insufficiency. It was observed that carbon dioxide content of the arterial blood exceeded 48 percent by volume in half of the patients with second stage respiratory insufficiency. Oxygen therapy in chronic hypoxia presents special difficulties since it entails a considerable disruption of carbon dioxide interchange. Additional CO_2 accumulation prevents development of the protective reactions which act to prevent hyperoxia. Data confirm that there are considerable disturbances of CO_2 interchange in chronic hypoxia Elimination of these disturbances should be an important aspect in treating this group of patients.

Soto, Rojas G., and C. Marquez. Some features of pulmonary insufficiency at high altitudes. Amer. Rev. Resp. Dis. 85:25-29 (Jan. 1962).

The results of pulmonary function tests (spirometry, blood gas analysis, mixed venous and arterial carbon dioxide, acid-base balance, hematocrit, and alveolar and arterial pO_2), performed in 65 patients with chronic pulmonary insufficiency and in 20 normal subjects in the altitude of the Mexican, plateau (7080 feet), showed that these patients were markedly unsaturated, and had very little carbon dioxide retention. Similar patients at sea level (with lowest pO_2) had pCO_2 levels at least 20 mm. higher. If pCO_2 rises very much in high-altitude patients, the oxygen falls to intolerably low levels.

Spadaro, O. Volume of circulating blood in Europeans acclimatized to Eritrean plateaus. Boll. Soc. Ital. Med. Trop. 4:913-918 (1944).

Specht, H., L.H. Marshall, and B. Hoffmaster. Effect of altitude on respiratory flow patterns. Amer. J. Physiol. 157:265-277 (May 1949).

Spinelli, N., P. Ceretelli, and G. Carrera. Effects of hypoxia and fatigue on cortical reflexes. Industr. Med. Surg. 32:14 (Jan. 1963). The present research studies variations in the cortical synaptic delay induced by different agents which are known to impair the performance of the subject.

Sserafimow, B. N. Influence of sojourn in mountains on resistance of erythrocytes. Folia Haemat. 54:261-267 (1936).

Sserafimow, B. N. Effect of sojourn in mountain region on vegetative nervous system. Z Ges. Phys. Therap. 45: 284-287. (1933)

Stammers, A. D. Polymorphonuclear - lymphocyte ratio at altitude of 5750 feet. J. Physiol. 78:335-338 (June 1933).

Starr. I., and M. Michael. Oxygen transport circulation and respiration in healthy subjects at simulated altitudes of 16,000 to 18,000 feet. J. Appl. Physiol. 1:430 (1948). Twenty-one healthy adult subjects were tested at sea level and at simulated altitude of 16,000 and 18,000 feet in a low pressure chamber. The subject sat in a ballistocardiograph built in the shape of an airplane pilot's seat. Blood pressure, respiration, and arterial oxygen saturation were measured and cardiac output and pulse rate were estimated from the ballistocardiograms. All these estimations could be made simultaneously. The increase in respiration and pulse rate and the diminution of arterial oxygen saturation at altitude coincided with expectations from previous work. The cardiac output increased by an amount sufficient to transport to the tissues, at altitude, a supply of oxygen which usually equalled or slightly exceeded that presented before ascent.

Steggerda, F.R., W.C. Clark, and J.E. Danhof. The continuous recording of tonic and activity pressure in the gastrointestinal tract at various altitudes: I. Factors affecting the tone and activity of the colon of man upon going to altitude. School of Aviation Med. Project No. 21-23-025, Report No. 1, Randolph AFB, Texas (March 1952). The tone and activity of the colon distended by 300 cc. of room air were measured at ground level and on ascent to simulated altitude of 12,000 to 25,000 feet. Inhalation of oxygen was commenced at 10,000 feet, and fluids were ingested at 12,000 and 15,000 feet. Ascent to 12,000 feet without fluids slightly decreased tone pressures and markedly increased colonic activity. Oxygen inhaled at 12,000 feet increased tone from 98 to 101 percent during 20- to 25-minute intervals and from 92 to 99 percent during a 40- to 45-minute interval; colonic activity increased 30 and 45 percent during the 20- to 25- and 40- to 45-minute interval respectively. Ingestion of water and milk produced an average increase of 49 percent in colonic activity compared to noninvestigation of fluids. A slight increase in colonic activity with ingestion of milk as compared to water was apparently caused by the secretagogue properties of milk. Increased colonic activity appeared to be due to gas distention and the resulting adaptation of the colonic musculature.

Steggerda, F. R., W. C. Clark, and I. E. Dankof. Motility and tone of the human colon at various simulated altitudes. J. Aviat. Med. 26(3):189-193 (June 1955).

Steward, L. R. Acute pulmonary edema of high altitude. New Zeal. Med. J. 60:79 (1961). A case of acute pulmonary edema occurring in a healthy young mountaineer and a case of mild pulmonary edema in a healthy person are presented. These are the two extremes of the Peruvian Andes "Soroche" or mountain sickness, and the acute form is a pulmonary edema from acute left ventricular failure, due to overexertion and anoxia. The exact physiological mechanism is not fully understood, but the process is a logical one.

Stickney, J. C., and E. J. Van Liere. Erythrocytes and hemoglobin values in acclimatization produced by discontinuous anoxia. Aviation Med. (13):170-176 (Sept. 1942). It was concluded that discontinuous exposure to anoxia is capable of producing a noticeable degree of acclimatization; the degree is measured by the amount of hemoglobin and erythrocytes, being directly proportional to the severity of the anoxia and its length of exposure.

Stickney, J.C., and E.J. Van Liere. Acclimatization to low-oxygen tensions in relation to gastric emptying. Amer. J. Physiol. 1:160 (Aug. 1942). The gastric emptying time of five dogs after a standard meal has been determined during continuous exposure to reduced oxygen tensions (100, 86, and 80 mm. Hg) corresponding to simulated altitudes of 12,000, 16,000 and 18,000 feet respectively. The usual delay in gastric emptying produced by anoxia has been found to be gradually reduced in every case. The return to normal gastric emptying time has been complete under these conditions at 100 mm. O_2 in four dogs and at 86 mm. O_2 in three dogs. At 80 mm. O_2, only one dog of the five has shown complete return to normal gastric emptying time.

Stickney, J. C., and E. J. Van Liere. Acclimatization to low oxygen tension. Physiol. Rev. 33:13-31 (1953).

Stirnemann, H. Experimental tetanus: comparative studies in high altitude and in the valley. Arch. Klin. Chir. 285(5):533-554 (1957).

Streit, K. Effect of climate in high altitude on number of blood platelets and in fibrin retraction. Pflueger Arch. Ges. 254(3):246-256 (Jan. 1951).

Strohlman, F. L., C. E. Rath, and J. C. Rose. Evidence for humoral regulation of erythropoiesis: studies on patient with polycythemia secondary to regional hypoxia. Blood 9:721-733 (1954).

Strass, H. Persistence of polyglobulin after return from high mountain sojourn (Valley disease). Folia Med. Int. Orient. 2:245-247 (1936).

Strauss, W., and C. Muller. Comparative study of insensible perspiration at low and at high altitudes. Z. Hyg. Infectionskr. 110:413-426 (1929).

Strickland, E. H., E. Ackerman, A. Anthony. Effects of altitude acclimatization on the equilibrium constant of rat oxymyoglobin. Amer. J. Physiol. 197(1):211-213 (1959). After continually exposing rats to simulated altitudes of about 20,000 feet for 2 months, studies were made of a possible adaptive shift in the oxymyoglobin equilibrium constant, K. The results indicated that cellular acclimatization does not involve changes in the value of K. The significance of this finding as it relates to the functional role of myoglobin during acclimatization is briefly discussed.

Strickney, J. C., and E. J. van Liere. Acclimatization to low-oxygen tension. Physiol Rev. 33:13-34 (1953).

Strohl, A., L. Binet, and B. Fournier. Responses of spleen to low barometer; polycythemia of altitudes. C. R. Soc. Biol. 97:148 (24 June 1927).

Strolo, M. An aspect of intellectual activity in hypoxia: experimental observations. Rev. Med. Aero. (Rome) 18(3):688-708 (July-Sept. 1955). The mental activity of 100 young adults (21 to 23 years) of the same professional and cultural level was tested at sea level (0 meters) and at a simulated altitude of 5500 meters in a decompression chamber. All subjects performed the task of simple subtraction. Hypoxia was found to affect both the mechanisms of mental activity and the graphologic psychomotor performances. Numbers became indistinct, coarse, larger, and out of proportion. An increased amount of corrections and percentage of errors was observed. This test appears to be of value in the selection of flight personnel who, on occasion, might be exposed to hypoxic conditions.

Strother, G. K., E. Ackermann, A. Anthony, and E. H. Strickland. Effects of altitude acclimatization on rat myoglobin; effect of viscosity and acclimatization on myoglobin reaction rates. Amer. J. Physiol. 96(3):517-519 (Mar. 1959). Equipment and procedure used in the determination of myoglobin-oxygen reaction rate constants in viscous

media are discussed briefly. The rate constants were determined for purified extracts of myoglobin from control and acclimatized rats over the viscosity range of 87 to 53 centipoise. Glycerol-water mixtures were used as the viscous media. The reaction rates were found to vary with the viscosity of the suspending medium in a nonlinear fashion. No difference was observed in the reaction rates for acclimatized virus control rats using skeletal muscle extracts. A preliminary investigation of heart muscle extracts indicates a decrease in the oxygen association for the acclimatized rats. The significance of the kinetic data is discussed.

Stroud, R. C., and H. Rabin. Changes in resistance to pulmonary blood flow due to altering the inspired gas tensions. Fed. Proc. 11:155-156 (Mar. 1952).

Strughold, H. Reaction of central nervous system and sensory organs at great height. Luftfahrt Med. Abhandl. 7:58-64 (1936).

Strughold, H. Atmospheric space equivalence. J. Aviation Med. 25:420-424 (Aug. 1954). In experiments simulating descent from altitude using subjects who were instructed not to swallow or make other movements that might ventilate the middle ear, it was found that pressure changes just perceptible to the middle ear were greater at very slow rates of descent than at the more rapid rates. Wide variations in thresholds of individuals were observed in the nine subjects tested. Threshold pressure changes for persistent middle ear pain were about 100 mm. Hg in the two subjects studied, irrespective of the rate of descent or the altitude at which descent was started.

Strumza, M. N. Physiology of flight at different altitudes. Rev. Prat. 13:2079-103 (11 June 1963).

Stutman, L. J., F. H. Kriewaldt, V. Doerr, and M. George. Effect of lipemia on arterial oxygen at high altitude. J. Appl. Physiol. 14:894-896 (Nov. 1939). Some of the effects of acute fat loading on arterial O_2 at high altitude are described. Five dogs were taken to 12,000 feet in an altitude chamber and given fat infusions (1 gm. per kg.) There was a 10-percent drop in the arterial O_2 content and a similar drop in the O_2 capacity. One of the dogs had a surgically induced intra-arterial septal defect and died of fat emboli. Three dogs serving as controls at ground level had a 4-percent drop in arterial O_2 content after fat infusions. The drop in the O_2 content and capacity of canine blood after fat infusions at 12,000 feet is at least twice that at ground level. A practical method is discussed for employing a fat tolerance test to screen poor human risks among flying personnel.

Subsuste, C., et al. Comparative study of the adrenal function at sea level and at high altitude: the response to ACTH. Air Force School of Aviation Medicine. Randolph Field, Texas, Report No. 58-95 pp. 1-17 (Sept. 1958).

Sulli, E., and A. Lobao. Changes in the number of erythrocytes and the hemoglobin value induced by the simultaneous action of intermittent anoxia, cobalt, and small blood transfusions. Rev. Med. Aero. (Rome) 20(2):224-234 (Apr.-June 1957). A marked increase in the number of erythrocytes was found in two groups of rabbits of the same sex, age, and on the same standard diet, under the simultaneous influence of intermittent anoxia, cobalt injection, and repeated small blood transfusions. The experiment lasted a month for each group. At the end of the experiment the increase in erythrocytes was 72.23 and 65.66 percent for groups 1 and 2, respectively, and hemoglobin also showed an increase of 45.52 and 20.22 percent respectively. A slight but insignificant increase in the hematocrit values was observed. This phenomenon demonstrates the importance of cobalt and blood transfusions as hematopoietic factors. Poikilocytosis and anisomicrocytosis were observed after each anoxia test.

Sulli, E. Effect of the duration of exposure to anoxia on the number of reticulocytes. Rev. Med. Aero. (Rome) 20(1):71-75 (Jan. -March 1957). In addition to polycythemia, prolonged anoxic anoxia in rabbits produced reticulocytosis which increased in intensity with the period of exposure to anoxia. This reticulocytosis did not appear to be dependent upon the severity of anoxia.

Sundstroem, E. S. Studies on adaptation of man to high altitudes. Univ. Calif. Publ. Physiol. 5:121-132 (1919).

Sundstroem, E.S., and G. Michaels. The adrenal cortex in adaptation to altitude, climate and causes. Memoirs Univ. Calif. (1942).

Sydnor, K. L., M. L. Sweat, G. Sazers, and H. B. Hale. Blood ACTH and corticosteroids in men exposed to environmental stress. AF School of Aviation Med., Report No. 55-22, Randolph AFB, Texas (April 1955). Blood ACTH and plasma adrenocorticosteroid titers were determined on nine groups of normal male subjects under the following experimental conditions: control subjects breathing air at room temperature for 15 or 45 minutes; subjects exposed to a simulated altitude of 14,000 feet (breathing 12-percent oxygen in an atmosphere of nitrogen) for 2, 15, or 45 minutes; subjects exposed to heat (120°F) for 15 or 45 minutes; and subjects exposed to

hypoxia and heat at 120°F for 15 or 45 minutes. The blood ACTH titer of one control subject was estimated to be 2.0 milliunits, that of one subject exposed to heat for 45 minutes was 0.75 milliunits, and that of the remaining 54 subjects was less than 0.5 milliunits per 100 ml. The mean 17-hydroxycorticosterone concentration in plasma of control subjects was 10.8 mg. and the mean concentration of corticosterone-like compounds was 5 mg. per 100 ml. The differences between the control and the experimental groups were not highly significant. It is concluded that the stresses employed did not appreciably activate the pituitary-adrenal system of these subjects.

Symous, P. H. Studies on erythrocyte, hemoglobin and iron content of blood of normal subjects at altitude of Witwatersrand (6000 feet). South African J. Med. Sci. 4:18-30 (Apr. 1939).

Syrotynin, M. M. The high-mountain expedition of the institute of clinical physiology of the Academy of Sciences of the Ukranian SSR in 1951. Pro vysokogirnu ekspedytsiiu instytutu klinichnoi Med Z. (Kiev) 23(2):3-5 (1953). At the altitude of 2000 meters members of the Mount Elbrus expedition experienced a state of excitement (stimulation), manifested as increased rate of movement of the hand, and tendency to fast speaking. At 4000 meters, nearly all persons began to suffer from mountain sickness, easy fatigability, headaches, sleepiness, and loss of appetite; one test subject lost consciousness. In persons with poor altitude adaptability, these symptoms were most marked; their pulse and respiration became irregular and the hemoglobin concentration was altered. After having reached the height of 4800 meters, the expedition descended, causing one of the participants to suffer changes in the higher nervous activity which, according to psychiatrist S. D. Pasiona, simulated hebephrenia. At 5300 meters, such symptoms were of a graver nature, appeared more frequently, and were accompanied by more severe manifestations of mountain sickness. Examination of the same persons five to seven days later showed signs of normalization, indicating a high degree of physiological acclimatization. No such changes in the physiological indices and in the higher nervous activity were observed among the staff members of the Mount Elbrus observatory who spent the winters atop the mountain. The second signal system was profoundly affected at 4250 meters in persons with inadequate processes of acclimatization. Changes in the higher nervous activity at high altitudes accompanied by frank mountain sickness indicate that a way can be found to alleviate the condition by means of preventive psychiatry. At high altitudes a change occurs in respiration: it acquires a periodic character, especially in sleep, when the cortical functions are inhibited. During a later expedition some of the test subjects were administered sodium amytal as an inhibitor of the cortical function of the cerebrum; under normal conditions this has no effect on the respiratory system, but at 2200 meters most of the tested individuals manifested a tendency towards periodic breathing.

Szasz, E. Excretion of iodine (in blood and urine) by normal and hyperthyroidic subjects in high altitudes. Med. Klin. 29:1584-1587 (17 Nov. 1933).

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Takacs, L. The circulation of limbs in hypoxic conditions. Acta Pysiol. Acad. Sci. Hung. (Budapest) 11(2):189-195 (1957). Arterial hypoxia was induced in dogs by exposure for about 95 minutes to an environment of 8- to 10-percent oxygen in nitrogen and the circulation in a hind limb studied. Blood flow in the limb increased slightly and vascular resistance decreased. The limb fraction of the minute volume also decreased. These findings were compared with hind-limb circulation in conditions of ischemic shock and dehydration.

Takacs, L., K. Kallay, and V. Vajda. The effect of acute arterial hypoxia on the organ blood flow in rats. Acta Physiol. Acad. Sci. Hung. (Budapest) 21(1):87-91 (1962). No change was found in cardiac output or in the distribution of blood flow between the heart, kidney, lungs, liver, intestines, and skin as measured by Saperstein's method.

Takacs, L., and M. T. Szabe. The mechanism of the metabolic changes in muscle during shock: A study of dehydration and arterial hypoxia. Acta Physiol. Acad. Sci. Hung. (Budapest) 11(1):67-73 (1957). In rats with arterial hypoxia induced by exposure to a 8- to 10-percent oxygen-nitrogen atmosphere, the level of adenosine triphosphate and glycogen decreased in the skeletal muscle, while the phosphorolytic and hydrolytic breakdown of glycogen remained unaffected.

Takacs, L. The metabolism of limbs in hypoxic conditions. Acta. Physiol. Acad. Sci. Hung. (Budapest) 11(2):197-203 (1957). The metabolism of the in situ limb was studied on dogs in ischemic shock, dehydration, and arterial hypoxia. In hypoxia, induced by exposure of the animals for 90 minutes to an environment of 8- to 10-percent oxygen in nitrogen, the oxygen consumption decreased while the glucose uptake was unchanged. Lactic acid output was slightly elevated.

Talbott, J. H. Pathologic effects (mountain sickness). Med. Physics :6-7 (1944). The etiology of chronic mountain sickness is probably diminished oxygen uptake by the body; the pathogenesis, however, is not known. The high concentration of circulation hemoglobin can be interpreted as a physiologic response, and is neither more nor less than that observed in non-affected residents at similar altitudes. Associated with an increase in hemoglobin is a decreased saturation of arterial blood. It is possible that a decade or more of persistent unsaturation of arterial blood is an integral part of the pathogenic mechanism.

Tappan, O. V., and B. Reynafarje. Tissue pigment manifestation of adaptation to high altitude. Amer. J. Physiol. 190(1):99-103 (July 1957). Guinea pigs native to Peru were used to study the myoglobin, hemoglobin, and cytochrome c content in tissue of animals at sea level and 14,000 feet. The pigments were extracted by various methods and the values read colorimetrically. The results show a significant increase in blood hemoglobin in the high-altitude animals, while cytochrome c and myoglobin show a smaller increase. A significant increase in myoglobin occurred only in some skeletal muscles, and in the heart and liver. Myoglobin, which could act as a vehicle for carrying oxygen or as a catalyst in oxidation, would, in greater amounts, raise the efficiency of oxygen utilization at high altitudes. An increase in cytochrome c could be advantageous to animals in oxidation reaction is at high altitudes.

Tappan, D. V., B. Reynafarje, V. R. Potter, and A. Hurtado. Alterations in enzymes and metabolites resulting from adaptation to low oxygen tensions. Amer. J. Physiol. 190(1):93-98 (July 1957). Succinoxidase activity has been demonstrated to be significantly higher in the tissues of guinea pigs native to altitudes of 14,000 to 14,900 feet than in sea-level guinea pigs. Desoxyribonucleic acid content is higher in the tissues of the altitude animals, indicating a larger number of cells per-gram of tissue, with a constant amount of succinoxidase activity per cell. Antimycin A titer, which varies little with altitude, and cytochrome c oxidase, which is increased in some tissues of altitude guinea pigs, indicates that altitude acclimation may be aided by increases in key reactions of enzyme series, avoiding the necessity for changes at all of the steps of the series. Altitude animals have increased glycolysis and adenosinetriphosphatase capacities and accumulate higher levels of high-energy phosphate. Animals moved from one altitude to the other show changes in enzyme concentrations indicative of acclimatization.

Tarasenko, V. M. Use of carbon dioxide at lowered barometric pressures Amer. Rev. Soviet Med. 2; 119-125 (Dec. 1944), and Klin. Med. (10-11) 19:39-47 (1941).

Telcharov, L. M., N. Nikolov, and St. Chernayev. Changes in the nervous system at an altitude of 2000 meters AFSC 65-17820. Foreign Technology Div., Wright-Patterson AFB, Ohio. At an altitude of 2000 meters, changes in the functional state of the human organism were observed in non-acclimatized subjects. The brain cortex activity was stimulated and the impulses were radiated to the centers of the autonomic nervous system, which caused an increase in neurovascular activity. The respiratory system was not affected to a significant degree, because the nervous system had sufficient power to maintain the necessary adjustment. However, a prolonged stay at high altitude could produce a permanent stress assuming pathological dimensions on the nervous system.

Tenney, S. M., H. Rahn, R. C. Strond, and J. C. Methoefer. Adaption to high altitude: changes in lung volumes during the first seven days at Mt. Evans, Colorado. J. Appl. Physiol. 5(10):607-613 (1953). The lung volumes of four subjects during a 7-day stay at 14,250 feet have been studied and the following trends observed. The vital capacity decreased during the first 3 days, then progressively increased in all subjects. The residual volume increased the first day, then fell during the next 4 days and had leveled off by the end of the week so that three subjects were above control values, and one subject was just at sea-level value. The total capacities were high initially, but by the end of the week two subjects had total volumes above those at sea level and two had volumes below sea level. The expiratory reserve volume increased progressively in all subjects over the first 6 days. Breathing oxygen in all four subjects and continuous positive pressure breathing in two subjects failed to increase the vital capacity. Certain implications of the lung volume changes, particularly in pulmonary blood volumes changes, are discussed.

Tenney, S. M. Physiological adaptions to life at high altitude. Mod. Conc. Cardiov. Dis. 31:713-8 (Mar. 1962). In response to the stress of hypoxia, man living at a high altitude makes use of a number of physiological processes which may be considered as adaptations. These processes can be described as serving to minimize the various partial pressure drops which oxygen undergoes in its passage from mouth to cell. The effectiveness may be judged from the fully acclimatized state to high altitude, where the partial pressure of oxygen in the venous blood is only slightly lower than at sea level, yet the inspired air may have a partial pressure of oxygen lower than is normally present at sea level. In addition to the contribution such observations provide toward a fuller understanding of the biology of man, the intrinsic mechanisms serve to elucidate many aspects of cardiorespiratory disease.

Terman, J. W., and J. L. Newton. Changes in alveolar and arterial gas tensions as related to altitude and age. J. Appl. Physiol. 19(1):21-24 (1964). In the summer of 1962 at the White Mountain Research Station, the early phases of altitude acclimatization were studied in six of the surviving eight members of the 1935 expedition to the Chilean Andes; they were from 58 to 71 years of age. Alveolar and arterial pCO_2 and pCO_2 were determined for each man a few hours after arrival at 3, 093 meters and at 3, 800 and 4, 343 meters over the next few days. The effects of age were superimposed on the classical responses to high altitude. The arterial and alveolar pCO_2 values showed no significant gradient; the alveolar pCO_2 was found to be lower for a given altitude than 27 years before. For example, their average alveolar pCO_2 at 4, 700 meters in 1935 was 27. 7 mm. Hg as opposed to 25.1 mm. Hg at 4, 343 meters in 1962. The case of Hall was exceptional: His alveolar CO_2 ranged from 21 to 24 mm. Hg regardless of altitude for his sojourn of 22 days. In 1935, these six men had a mean A-a PO_2 gradient of +3.0 mm. Hg at 4, 700 meters, while in 1962 the gradient over the three altitudes was +12.4 mm. Hg. It is probable these findings can be partially explained by age changes in the pulmonary ventilation-perfusion ratio.

Terzioglu, M. N., F. Ozer, and A. Songar. Studies in blood physiology at mid-altitude: I. Variation in blood morphology at Uladag (1850 m.) Arch. Int. Physiol. (Paris) 60(3):233-252 (1952). The progress of erythropoiesis and related processes was observed on 11 subjects over a period of 10 days at Uladag (Turkey) (elevation 1850 meters, atmospheric pressure 610-617 mm. Hg.). The erythrocyte count increased 10.9 percent and the hemoglobin concentration 8.6 percent within 10 days. Only very slight deviations of the blood color index from normal were observed. The percentage of total red cell volume rose during the first 3 days. The erythrocytes diametric decreased initially, but returned to normal at the end of the 10-day period. At the beginning, the resistance of the erythrocytes to hypotonic solutions was below normal; the resistance increased, however, after a few days of altitude exposure. Upon return to sea level, hemoglobin concentration, hematocrit value, and corpuscular volume returned to normal within 8 to 10 days, while the mean corpuscular surface area remained high. The osmotic resistance of the erythrocytes increased still further. The physiological mechanism of the observed changes is discussed.

Terzioglu, M. N., N. Pekoz, and F. Ozer. Studies in blood physiology at mid-altitudes: II. The gaseous content and acid-base equilibrium of blood at Uladag (1850 m.). <u>Arch. Int. Physiol.</u> (Paris) 60(3):252-265 (1952). O_2 and CO_2 contents, O_2 capacity, alkali reserve, and pH values of venous blood were measured on 2 female and 8 male students during a 10-day stay at Uladag, Turkey (1850 meters altitude). The venous O_2 content decreased 32.3 percent within 10 days, while the O_2 capacity remained unchanged. There was a marked decrease in the O_2 saturation of venous blood while erythropoietic changes were in progress, a fact that suggests a correlation between erythropoiesis and anoxemia. The blood pH remained unaltered, but the alkali reserve decreased from the beginning of the stay. All values returned to normal within 8 to 10 days after return to sea level. A physiological interpretation of the data is attempted.

Terzioglu, M., F. Oeger, and N. Gokhas. Plasma and erythrocyte level of human blood bicarbonate and chloride ions at an altitude of 1950 meters. Minerva Med. (Turin) 47(53):14-16 (4 July 1956). No significant changes were observed in the distribution of cellular and plasma bicarbonate in subjects staying at Uludag, Turkey (1850 meters of altitude) for 11 days. The plasma chloride ion remained unchanged, but erythrocyte chloride content increased by 7.4 and 5.4 percent in two experimental periods. During the first few days at altitude, plasma water content decreased, but cellular content increased. Total blood values for bicarbonate and chloride ions showed a decrease by 7 and 5.3 percent of the bicarbonate values, and an increase of 2.9 and 1.9 percent of the chloride values in two experimental periods. On the basis of these results, the decrease in alkaline reserve at altitudes cannot be explained in terms of the redistribution of alkaline ions between blood and tissue as a result of increased loss of carbon dioxide from the alveolar surface.

Terzioglu, M, and A. Tuna. Variations in blood volume at 1.85-km altitude. J. Appl. Physiol. 6(7):417-422 (Jan. 1954). To investigate the hematological variations at mid-altitude, blood volumes of seven experimental subjects before, twice during, and after a 10-day sojourn at Uladag, Turkey (1850 meters). The plasma volume remained practically unchanged during the period at mid-altitude. Nine to ten days after descent to sea level, the plasma volume increased to 6.9 percent over the initial value, indicating a hemodilution. Total blood volume had increased 7.5 percent by the end of the 10-day period at mid-altitude. This increase occurred at about the same time as other hematological variations previously observed, and was mainly due to an increase in the total blood volume. The total blood volume was greater than the pre-expedition value, but less than the final mid-altitude value. This relatively high blood volume resulted chiefly from the increase in plasma volume, since the total cell volume was practically normal. By the end of the 10-day period at mid-altitude, total blood volume and total cell volume was 10.2 and 17.8 percent respectively above preexpedition values. On return to sea level, the total amount of circulating hemoglobin remained at mid-altitude values, while the cell volume decreased.

Terzioglu, M., and R. Aykut. Variation in basal metabolic rate at 18.5 Km. altitude. J. Appl. Physiol. 7(3):329-332 (Mar. 1959). The basal metabolic rates of 12 experimental subjects (20 to 23 years of age) were determined at various periods during a sojourn of 12 days at (Uladag) (1850 meters). These values have been compared with those obtained at sea level (Istanbul) prior to ascent and following the descent from mid-altitude. The basal metabolic rate of each subject was expressed both as cal/24 hour and cal/M^2/hr. Both values were definitely increased on the fifth to the sixth day of the test at Uladag and remained at practically the same level during the remainder of the experimental period on the mountain. On return to sea level, the basal metabolic rate was reduced to normal in all subjects within various periods of time following the descent from mid-altitude.

Terzioglu, M., F. Ozer, and N. Gokhan. Variations in gaseous content and acid-base equilibrium of arterial blood at 1.85 km. altitude. J. Appl. Physiol. 6;7:423-428 (Jan. 1954). O_2 and CO_2 contents, O_2 capacity, pH, alkali reserve, and lactic acid amount of arterial blood in seven healthy male subjects (21 to 29 years of age) were determined during a period of 10 days at Uludag (1850 meters). These values are compared with those obtained at sea level prior to ascent and following descent from the mountain. From the values for O_2 content and O_2 capacity, the percentage O_2 saturation was computed. By the end of the expedition to Uludag, O_2 capacity had increased 10.1 percent over sea level value. Hemoglobin concentration increased about the same magnitude. These findings confirm the authors' previous results regarding the onset of erythropoiesis at mid-altitude. The mean percentage O_2 saturation in arterial blood was diminished about three percent below the sea level average during both data collection periods at Uludag. From the O_2 dissociation curve of Bock et al, this diminution corresponded to a reduction of about 24 mm. Hg in pO_2. This finding as well as the augmented lactic acid content at mid-altitude was interpreted as indicating a state of partial anoxia in the tissue and as offering sufficient evidence of an accelerating effect on erythropoiesis by H+ions accumulated in the bone marrow.

Terzioglu, M. Influence of chemoreceptor denervation and subsequent discontinuous anoxia on erythropoiesis and acid-base equilibrium in the rabbit. Amer. Jour. Physiol. 182(1):100-104 (July 1955). Changes in erythropoietic response and acid-base equilibrium under hypoxia were studied in rabbits after denervation of the carotid and aortic areas. Intermittent exposure to environmental pressures of 400-410 mm. Hg produced an intense polycythemia with increases in erythrocyte count and hemoglobin concentration continuing for 150 hours after exposure. Reticulocyte counts, elevated initially by denervation, remained at a high level for 50 hours after exposure. Unilaterally denervated animals showed an increased erythropoiesis midway between the response of bilaterally denervated animals and that of controls. Inhalation by denervated animals of an 8.5 to 10.5 percent O_2 mixture for short periods caused the percentage of O_2 saturation in arterial blood to fall to levels existing in venous blood. A rise in blood pH occurring with an increase in CO_2 content was attributed to decreased oxygen saturation and the subsequent presence in the blood of greater amounts of reduced hemoglobin.

Theilen, E. O., D. E. Gregg, and A. Rotta. Excercise and cardiac work response at high altitude. Circulation. 12(3):383-390 (Sept. 1955).

Theilen, E. O., M. H. Paul, and D. E. Gregg. Cardiac output determinations with the cuvette densitometer: techniques for blood of reduced oxygen saturation. Amer. J. Physiol. 179:679 (1954). The response to treadmill exercise of the left ventricle of natives of the regions of Marococha, Peru (elevation 14, 900 feet), was studied. In both groups the external work of the left ventricle was affected by a combination of a large increase in cardiac output and a mild increase in systemic blood pressure. Stroke volume and stroke work were only mildly elevated since the heart rate was concurrently greatly increased. As a result, the increase in work of the left ventricle was largely accomplished by an increase in heart rate and to a lesser extent by an increase in stroke work. For comparable amounts of external work, theventricle of the high-altitude native performing at high altitude responded with considerably greater effort than did the left ventricle of the low-altitude native performing at sea level. Some of the data may have approximated the maximum effort of which the normal left ventricle was capable.

Therien, M. Respiration at high altitude. Laval Med. 14:797-808 (June 1949).

Thilenius, O.G. Response of pulmonary circulation of resting, unanesthetized dogs to acute hypoxia. Amer. J. Physiol. 206:867-874: (Apr. 1964). In nearly all of 54 experiments with 5 dogs, there were striking responses to hypoxia (breathing 6 to 15 percent O_2), consisting of a marked rise (up to 12 percent) in pulmonary artery pressure (PAP), in cardiac output (Q) up to 200 percent, and a significant fall in left-atrium pressure (LAP). In some animals these changes were not maintained throughout hypoxia. The pulmonary vascular resistance (PVR) was usually the first to return toward normal, followed by PAP, while Q remained elevated. The time sequence of these events varied in different animals. Effects of the same magnitude as in hypoxia accompanied restlessness caused by stress, but fluctuating markedly, were of shorter duration, and could largely be eliminated by providing quiet surroundings and avoiding prolonged experiments. It was concluded that active vasoconstriction occurs in the pulmonary vascular bed during acute hypoxia in the intact unanesthetized dog. Normal values for PAP, Q, and PVR for resting, waking dogs are also reported.

Thomas, P. K., et al. Influence of hypoxia on the thermal homeostasis man. Lovelace Foundation for Med. Education and Research, AD288685, Albuquerque, N. Mex. The influence of induced hypoxia on core and shell-temperatures, metabolic rate, perspiration and other related cardiopulmonary parameters was studied in six healthy subjects under neutral, cold, and warm environmental conditions. In all three environmental conditions (with room mean skin temperatures air breathing) are not different from those in similar environmental conditions with hypoxia. It is concluded that a hypoxic level o tracheal O_2 = 65 mm. Hg does not appreciably influence mean skin temperatures in a neutral, cold, or warm environment. Rectal temperatures during hypoxia are not different from that during room air breathing in neutral and cold environments. However, this is not 'rue in a warm environment, where rectal temperatures are significantly higher during hypoxia than during room air breathing. The mechanism of this phenomenon cannot be explained on the basis of thermal balance alone. No great influence of hypoxia on shivering or perspiration can be detected under the experimental conditions. The synergistic actions of hypoxia and thermal stresses on total ventilation and heart rate are demonstrated.

Thorn, G. W., et al. The role of the adrenal cortex in anoxia: the effect of repeated daily exposures to reduced oxygen pressure. Amer. J. Physiol. 137:606 (1942). Armstrong and Heim first called attention to changes which occurred in the adrenal glands of rabbits exposed repeatedly to low pressure. In their experiments young male rabbits were exposed in a decompression chamber to a pressure equivalent to an 18,000-foot altitude for 4 hours daily, 5 days each week. This experiment was an attempt to confirm the findings of Armstrong and Heim with respect to the changes in the adrenal glands of exposed animals and has, in addition, extended the studies to include observation in other physiological and biochemical changes which occurred in animals subjected to repeated daily exposures to reduced oxygen pressures.

Thorn, G. W., M. Clinton, B. M. Davis, and R. A. Lewis. Effect of adrenal cortical hormone therapy on altitude tolerance. Endocrinology 36:381-390 (1 June 1945). Treatment with a concentrated adrenal cortical extract in oil increased significantly the survival rate of normal rats exposed to a standardized acute altitude tolerance test. The mechanism accomplishing this improvement is not known.

Thorner, M. W., and F. H. Lewy. The effects of repeated anoxia on the brain; a histopathologic study. J. A. M. A. 115:1595 (1940).

Thorner, M. W. A study of cerebral physiology at high altitude. AF School of Aviation Med. Project No. 60, Report No. 1 (Mar. 1943).

Thorner, M. W. The effects of altitude chamber anoxia upon the human electroencephalogram. AF School of Aviation Med. Project No. 119, Report No. 1 (Feb. 1943).

Timiras, P. S., R. Hill, A. A. Krum, and A. W. Lis. Carbohydrate metabolism in fed and fasted rats exposed to an altitude of 12,470 feet. Amer. J. Physiol. 193(2):415-424 (May 1958). Blood sugar levels and the glycogen content of liver, heart, skeletal muscle, diaphragm, and kidney of both fed and fasted sea-level control rats were compared with those of fed and fasted rats (P) born at sea level and then exposed to an altitude of 12,470 feet for various periods of time, and with those of fed rats of the second filial generation (F_2) born and maintained at altitude. In the P animals after short-term (24 and 72 hours) exposure, liver heart, muscle, and diaphragm glycogen was markedly decreased in the fed animals as compared with the fed sea-level controls, and markedly increased in the fasted hypoxic animals as compared with the fasted sea-level controls.

In fed P animals after long-term exposure, liver, heart, muscle, and diaphragm glycogen was the same as in fed controls after 2 and 6 months at altitude, and became markedly lower than in the controls after 10 months. In the F_2 rats, liver and muscle glycogen was markedly decreased when compared with the controls; in contrast, cardiac glycogen was significantly higher in F_2 rats than in the controls. Changes were not observed in kidney glycogen. Hyperglycemia was observed in all P rats after 24 hours, and hypoglycemia after 72 hours at altitude. In the long-term experiments, glycemia was the same in experimental (P and F_2) and control rats.

Timaras, P. S., N. G. Pace, and C.A. Hwang. Plasma and urine 17-hydroxycorticoid and 17-ketosteroids level in man during acclimatization to high altitude. Fed. Proc. 16:340 (1957).

Timiras, P. S., A. Krum, and N. Pace. Body and organ weights during acclimatization to an altitude of 12,470 feet. Amer. J. Physiol. 191(3):598-604 (Dec. 1957). Body and organ weights of rats kept at sea level were compared with those of rats (P) born at sea level and then exposed to 12,470 feet and with those of rats of the second filial generation (F_2) born and kept at 12,470 feet for periods up to 10 months. Body weight for the F_2 rats was lower the first day of age than in either the sea-level or P rats. Weight gain dropped in the P rats at 72 hours, became normal at 1 week to 6 months and dropped again after 7 to 10 months. Weight gain in the F_2 rats dropped from normal after 5 days and always remained smaller than in the sea-level or P rats. Cardiac hypertrophy in the P rats occurred after 10 months of exposure, and hemoglobin values increased after 2 months. A 40-percent increase of adrenal weight was accompanied by thymic and lymphatic atrophy, but these changes did not occur in the F_2 rats.

Timiras, P. S. et al. Endocrine responses during adaptation to moderately high altitude. Abstract in Fed. Proc. 15(1, part 1):187 (Mar. 1956). Studies of various organs were made in rats exposed for various periods of time at the 12,500 foot level of the White Mountain Research Station, California (P animals), in rats of the second generation born at the station (F_2 animals), and in rats remaining in the parent colony on the Berkeley campus (sea level controls). After one to three days of exposure, adrenocortical activity was simulated as indicated by a 40- to 50-percent increase in adrenal weight; a loss of adrenal ascorbic acid (after 1 day's exposure), and a 60- to 80-percent decrease in weights of thymus, spleen, and lymph nodes. No changes in weights could be observed in hypophysis, testes, and thyroid. The glands were significantly enlarged after

three days of exposure. After a two-month exposure, the P animals showed a significant enlargement of the hypophysis and thyroid as well as of the adrenals even when other criteria (e.g., growth, reproduction, blood hemoglobin and hematocrit) indicated adaptation to the new environment. Testes and preputial glands remained unchanged. On the other hand, in the F_2 animals born at high altitude, endocrine weights appeared to be similar to those of sea level controls.

Tinney, W. S., E. Hall, and H. Z. Giffin. The liver and spleen in polycythemia vera. Proc. Mayo-Clin. 18:46 (1943).

Torres, E. D. Cardiovascular response to effort in Andes. Med. Depor. Trab. 10:590-594 and 598-600 (Feb. 1947).

Trapani, I. L., and D. H. Campbell. Passive antibody decay in rabbits under cold or altitude stress. J. Appl. Physiol. 14(3):424-426 (May 1959). Rabbits maintained at an environmental temperature of 15°C (5°F) for 10 weeks exhibit an increase in the decay of passively administered antibody. Rabbits acclimatized at an

altitude of 12,470 feet for 30 days show little or no change in passive antibody decay. Protein turnover in these groups of animals is discussed.

Trebrukait, B. Readaptation of the rat with high altitude polycythemia to sea level. Acta Physiol. Scand. 57(4):419-430 (Apr. 1963). Rats were submitted to hypoxia corresponding to 6000 meters altitude for 40 to 50 days. The total amount of hemoglobin, blood volume, and relative blood values (hemoglobin concentration and hematocrit) had been studied in hypoxia and after transfer to normal oxygen pressure. Total hemoglobin increased during hypoxia by 150 to 200 percent, relative blood values by 100 percent, and blood volume by 25 to 50 percent, indicating the increase of oxygen capacity of the blood and the volume of the circulatory system. Thirty days after transfer to normal oxygen pressure, total hemoglobin, blood volume, and relative blood values had returned to normal. Thereafter, relative blood values showed a transient decrease, but not the total hemoglobin. Thus the blood volume increased again. Problems in connection with the homeostatic regulation of erythropoiesis are discussed. The body weight decreased during hypoxia by about 15 percent. After the period of hypoxia the rate of increase in body weight was faster than that of animals of the same order and body weight.

Tribukait, B. Arterial HbO_2 saturation and alveolar CO_2 and O_2 pressure in rats in altitudes of 2 to 7000 M. Acta Physiol. Scand. 58:90-8 (May 1963)

Tyurin, A. M. Value of oxyhemometric determination of blood flow rate and oxidation level in appraising acclimatization to high-mountain conditions. AFSC No. 65-17821, Foreign Technology Div. Wright-Patterson AFB, Ohio. Clinical examinations of a group of Soviet skiers training for the Olympic games at an altitude of 1500 to 2000 meters disclosed the following physiological changes: pulse rate was decreased, blood pressure was lowered, hemoglobin content values were lower than normal, blood flow rate was increased, oxygenating process was more intensive, and fatigue-recovery time was shortened.

Tschirren, B., and K. Wiesinger. Temporal course of consensual pupillary reflex during ascent to high mountains. Helvet. Physiol. Acta Pharmacol. 6:554-559 (1948).

Tsyrul'nikov, A. N. Changes in circulation and blood O_2 saturation during acclimatization of man to mountain conditions. Bull Exp. Biol. Med. 52:903-907 (Feb. 1962). Acclimatization of the cardio-vascular system was observed in a group of highly trained alpinists

during ascent to Peak Pobedy (7439-meters altitude). Fourteen days were spent at the 7000-meter altitude without O_2 apparatus. At high altitude (6200-meters) the pulse rate reached 89.4 beats per minute on the first day; it decreased on the third day to 85 beats and in some cases to 70 beats. At the 7100 meter altitude, the pulse rate after 4 days of acclimatization averaged 108 beats per minute and in some individuals was as low as 90 beats per minute. Systolic arterial pressure showed no change, while the diastolic pressure occasionally was decreased. Function tests at high altitude indicated a favorable response of the cardiovascular system to acclimatization. Oxyhemometric measurements were taken before, during, and after holding breath. Average time of breath holding ranged between 3 and 4 minutes. Acclimatization permitted O_2 saturation of blood to fall to lower levels before resumption of breathing and reduced the restorative period. It is concluded that trained and acclimatized mountain climbers are capable of considerable physical exertion at high altitudes without any untoward shifts in the cardiovascular respiratory systems.

Tuba, J., and O. Rorcher-Mayr. Studies regarding control and promotion of altitude training at Obergurgl. Wien. Klin. Wschr. 66:919-921 (Dec. 1954). Comparative studies were undertaken on acclimatized (trained and untrained) subjects and acclimatized natives at the

Obergurgl Alpine Research Station (2000 meters) for the medical control and promotion of mountain training. It was shown that athletic proteinuria was frequently encountered in trained but unacclimatized subjects after exertion, except in the morning hours. An increased morning urobilinogenuria and proteinuria was observed in a significant number of untrained and unacclimatized subjects. It was concluded that athletic albuminuria unaccompanied by an increase in the total lymphocyte count may be explained not only by lack of physical training or exertion, but also by insufficient acclimatization to altitude, as substantiated by frequent albuminuria in physical education students. A comparison of diurnal variations in the leukocyte profiles showed a significant evening rise in the unacclimatized subjects. The lymphocyte-leukocyte profiles showed a significant evening rise in the unacclimatized subjects. The lymphocyte-leukocyte count remains on the same level (but slightly higher) for the acclimatized natives. The choline citrate and calcium citrate diet supplement, tested in connection with research on acceleration of acclimatization to altitude, lowered the diastolic blood pressure through peripheral vasodilation.

Turanov, V. V. On the problem of adaptation of adult human organism to oxygen insufficiency. AFSC N 65-17775, Foreign Technology Div., Wright-Patterson AFB, Ohio. Experiments were conducted on the same individuals, both in the decompression chamber and at high altitude. At moderate elevation (below 3000 meters), the first response to hypoxia was that of the respiratory system. The minute respiratory volume was increased by the increase in the tidal volume; respiratory rate and cardiac rate remained normal at higher elevations (above 3000 meters); the pulse rate increased; the red blood count and hemoglobin concentration showed higher values than normal. At the 3000-meter altitude the response was due to the activity of the cerebral cortex. The electrocardiogram showed a decrease in the T-P interval, and an increase in the R-wave magnitude. The drop in the oxygen tension of the peripheral blood was not sufficiently compensated by the increase of the red count and hemoglobin content. As a result, the subject experienced discomfort. During sleep or under anesthesia, the activity of the adaptive mechanisms was retarded.

Tupusbekov, B. T. Mechanisms employed by the organism to adapt to high-altitude conditions. AFSC N 65-17818, Foreign Technology Div., Wright-Patterson AFB, Ohio. The first phase of adaptation to hypoxia is nervous stimulation of hemodynamics and respiration. During the second phase the specific (oxygen deficiency) and nonspecific (pressure, temperature, humidity, and illumination) stimuli are differentiated, resulting in the adjustment of organic functions. The third phase combines the further development and improvement of functions with structural changes, which could be passed on to the next generation. Unlike experimental conditions of simulated constant pressures, the natural conditions vary from day to day. Therefore, the natural process of adaptation to high altitudes proceeds unevenly under the effect of specific and nonspecific factors.

Tynybekov, A. T. Arterial pressure norms for native inhabitants of the mountainous regions of Kirgizia. AFSC N 65-17835, Foreign Technology Div., Wright-Patterson AFB, Ohio. Comparative studies of blood pressure values of inhabitants of the lowlands and of the Kirgizia mountains disclosed that blood pressure levels were lower in the residents of the Kirgizia highlands than in the inhabitants of Leningrad or Moscow, as far as individuals under 29 years of age were concerned. Older persons, however, did not show such variations.

U

Uihlien, A., and W.M. Boothly. Hyperventilation: its occurrence among passengers on airplanes. Proc. Mayo Clin. 17:417-419 (1942).

Ullman, E.A. Renal water and cation excretion at moderate altitude. Abstract in J. Physiol. (London) 120(4):58p-59p (1953). Water and metabolism were studied in one healthy subject during 12 days in London, 29 days on the Jungfraujoch (11,340 feet: barometric pressure approximately 500 mm. Hg) and a further 14 days in London. No symptoms of altitude sickness were experienced at any time. Voluntary or anoxic hyperventilation of short duration at sea level leads to an immediate increase in renal sodium, potassium, and water output, a markedly accelerated water diuresis, a rise in urinary pH, and a fall in the excretion of ammonia and titratable acid. During the first two days on the Jungfraujoch, water, sodium, and potassium excretion were strongly depressed. On the third day, a sodium diuresis began, which lasted for three days. The daily sodium balance became negative (mean, 42 milliequivalents per day) and water and weight were lost in spite of a high caloric intake. From the sixth to the twenty-ninth day no further significant disturbance of water

balance occurred. After the sixth day on the Jungfraujoch, renal potassium excretion increased progressively. The findings suggest a possible increase in adrenocortical activity at altitude. The stimulus for the initial inhibition of water and fixed base excretion cannot be attributed to anoxia or alkalosis but was probably due to some non-specific factor connected with change of environment, perhaps, acting through release of antidiuretic hormone from the posterior pituitary. This theory is supported by the same sequence of events occurring on return to sea level.

Ullrick, W. C., W. V. Whitehorn, B. B. Brennan, and J. G. Krone. Tissue respiration of rats acclimatized to low barometric pressures. J. Appl. Physiol. 9(1):49-52 (July 1956). The tissue respiration rate of rats acclimatized to a simulated altitude of 18,000 feet for an average of 11.2 weeks was determined by the Warburg technique under 100-percent oxygen. Acclimatized animals showed increases in hemoglobin values and heart-body weight ratios, but no significant alterations from normal in growth rate, total metabolic rate, and rectal temperatures. No significant changes were observed in the tissue respiration rates of brain, small intestine, diaphragm, liver, skeletal muscle, atrium, and ventricle. Adrenal-body weight ratios were unchanged, but increased adrenocortical activity was suggested by a significant increase in adrenal oxygen consumption. The respiration rate of kidney slices was reduced. It is concluded that a generalized adaptation of cellular metabolism to high altitude does not occur but that changes may be demonstrated in tissues specifically involved in the adaptation process.

Ungehener, H. Climatic characteristics of mountains. Arch. Phys. Ther. 6:189-194 (May-June 1954).

Ulovich, A. I. Decrease in the organism's resistance to oxygen starvation under the influence of narcotics. AFSC NA65-1777, Foreign Technology Div., Wright-Patterson AFB, Ohio. The resistance of narcotized animals to moderate degrees of oxygen starvation was investigated and led to the observation that the survival rate of narcotized animals decreased in both anemic and hypoxic hypoxia. Respiration blood pressure and oxygen contents in arterial blood of cats and rabbits indicated sharper deviations from the initial physiological level in narcotized animals as compared with those that were not drugged. The rhythm of respiration was also disturbed in animals narcotized with sodium amytal and chloralose. However, data taken during this experiment were not conclusive and the general conclusion that narcotics have a positive effect in oxygen starvation is not warranted.

Unti, O., and A. S. Ramos. Anophelism of high regions of Southern **Brazil.** Arg. Hig Saude Pub (Sao Paulo) 7:89-106 (May 1942).

V

Vacca, C., and E. Boeri. Variations in the activity of muscular lactic dehydrogenase in rats subjects to prolonged hypoxia. Med. Aero. (Paris) 10(1):47-49 (1955).

Vacca, C. The restoration time of muscle contraction in conditions of hypoxia. Riv. Med. Aero. (Rome) 15(3):376-387 (1952). Healthy male subjects were given a weightlifting test (3 to 5 kg. lifted 3 cm. higher-per-second by the second phalanx of the middle finger of the right hand) in a decompression chamber. The experiments were carried out at ground level and at simulated altitudes of 3500, 4500 and 5500 meters. According to the myographic fatigue curve, the same time periods were required to induce fatigue and to restore muscle contraction at sea level as at altitude. Chemical variations of the blood were analyzed at all four altitude levels. The pyruvic acid concentration had a tendency to decrease at higher altitudes, especially under the influence of work. Lacticemia at rest in anoxia did not show high values but increased after muscular fatigue and persisted even after restoration of muscular contraction. Oxygen breathing decreased the lactic acid content of the blood but increased slightly the pyruvic acid level.

Vacek, T. Functional adaptation of heart in mice living under insufficient oxygen supply. Arch. Ges. Physiol. 212:357-364 (1926).

Vakar, M. L., et al. Changes of blood oxygen at high altitudes and their relation to the effectiveness of a space suit. Voen. Med. Zh. (Moscow) 5:29-32 (May 1959).

Velasquez, T. Maximal diffusing capacity of the lungs at high altitudes. School of Aviation Med., Report No. 56-108, Randolph AFB, Texas (1956).

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Van Liere, E. J. Anoxia: its effect on the body. Chicago: University of Chicago Press, 1942.

Van Liere, E. J. Effect of prolonged anoxemia on the heart and spleen in the mammal. Amer. J. Physiol. 2:290-294 (July 1936). Fifteen guinea pigs were kept at low oxygen tensions for periods varying from 20 to 105 days. The oxygen percentages ranged from 12.25 to 10.50 percent. It was found that the average heart weight to body weight ratio was increased to 155.8 percent of the normal value. The

average spleen weight to body weight ratio in nine animals increased to 531.0 percent of the normal value. Owing to the polycythemia caused by the low oxygen tensions, the spleen would have to destroy many red blood cells and it is suggested that this might well account for the increased size of this organ. The hypertrophy of the heart could have been caused either by a work hypertrophy or an injury hypertrophy or, perhaps, by a combination of both. This study lends experimental evidence to the observations made by Strohl that rarefied atmosphere is capable of producing cardiar hypertrophy.

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Van Liere, E. J., G. Crisler, and J. A. Wiles. The effect on anoxemia on the pyloric sphincter. Amer. J. Physiol. 2:330-334 (Mar. 1935).
In a series of barbitalized dogs it was found that anoxemia caused a rise in tone of the pyloric sphincter in some animals and a fall in tone of others. In a few animals, anoxemia caused a rise at one time and a fall at another. As a rule, the height of the pyloric contractions, was diminished by anoxemia especially if severe grades were used. In some instances, anoxemia produced an initial stimulation, so that the contractions were actually higher, although this was generally followed by a subsequent depression. This variability in the results

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investigators using sea-level residents, this study indicates that the native resident of an altitude of 14,900 feet has a greater tolerance to acute hypoxia than the native sea level resident. A discussion is provided on the relative influence of hypoxia and hypercapnia on the symptoms which developed during this test.

Velasquez, T. Correlation between altitude and consciousness time in high-altitude natives. AF School Aviation Medicine, Report No. 60-8, Randolph AFB, Texas (Dec. 1959). This study investigates the duration of consciousness in high-altitude natives breathing air at altitudes ranging from 32,000 to 40,000 feet, and constructs a correlation curve between the consciousness time and the altitude reached.

Velasquez, T. Diffusing capacity of the lungs at high altitude. AF School of Aviation Med., AD 128 585, Randolph AFB, Texas, (March 1956). The maximal diffusion capacity (DO_2) of the lungs during submaximal physical activity at two levels of oxygenation was determined in 12 native residents of Marococha, Peru (altitude of 4540 meters). A different degree of exercise was used in two groups of subjects and no relationship was observed between the oxygen consumption and the DO_2 value. The DO_2 values were found to be

consistently higher than values observed at sea level by several investigators who used similar measurement techniques. An interpretation of this finding, which represents an adaptative mechanism to the low pressure environment, has been attempted on the basis of various physical and physiologic characteristics present in the high-altitude residents.

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exertion counteracted the development of arterial hypoxia, but inhalation of oxygen-poor air i.. ıced hypoxia even during light muscular exertion. The ability of the organism to counteract the development of hypoxia during muscular exercise, especially under conditions of low oxygen tension, depended upon the rate at which the organism compensated for the high oxygen consumption by appropriate adjustments in respiration and blood circulation. In this respect physical training played a prominent role.

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Foreign Technology Div., Wright-Patterson AFB, Ohio. The oxyhemoglobin dissociation curve was studied in several generations of rats kept in environmental chambers and subjected to hypoxia by maintaining the ambient air at a constant composition of 89.5 percent N_2 and 10.5 percent O_2 at normal pressure. Hypoxic animals of the eleventh to thirteenth generation showed a shift in the oxyhemoglobin dissociation curve in 55 to 57 percent of the cases. In the majority of cases, the shift was to the left in the area of the upper inflexion, and in 30 percent of the cases, it was to the right in the area of the lower inflexion. In some cases, the shift was noted simultaneously to the left in the upper inflexion and to the right in the lower inflexion area. The oxyhemoglobin dissociation curves indicate the respiratory function of blood and the hemoglobin affinity to oxygen, and may serve as indices of the greatest degree of adaptation to hypoxia.

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zation to high altitude; observations made on the British Expedition to the Colombian Andes, Jan. 1957. School of Aviation Med. Report No. 58-79 pp. 1-15 (Aug. 1958). The expedition plan was based on the clinical and experimental evidence, that alkalosis tends to produce potassium depletion, and, conversely, that potassium deficiency tends to enhance alkalosis. These two processes acting together may set up a vicious cycle, of which examples occur in clinical practice (e.g., pyloric steriosis). In mountain sickness, the same two factors may be at work: alkalosis is produced by overbreathing; and anoxia may lead to some degree of potassium depletion. Supplying potassium, so that the kidney can make its own adjustment of acid-base balance, is the logical method of breaking the cycle. Observations during this expedition, as far as they go, fit in with this theory.

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oxygen saturation was marked, moderate, and minimal in patients inhaling oxygen concentrations of 110, 130, and 150 mm. Hg, respectively.

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West, J. B. Oxygen transfer by the lung at high altitude. Presented at the International Congress of Physiological Sciences, Leidin, 1962. Proceedings, 2(297): Amsterdam, 1962. During the Himalayan Scientific and Mountaineering Expedition, 1960-1961, the diffusing capacity of the lung for carbon monoxide was measured at 19,000 feet (approximately 380 mm. Hg) at work levels of 300 and 900 kilograms per minute. A difference in diffusing capacity of less than 20 percent compared with sea level values was found, which could be wholly accounted for by the increased rate of reaction of carbon monoxide with hemoglobin due to hypoxia. Measurements of arterial oxygen saturation by ear oximetry gave an average resting value of 67 percent which fell to 63 and 56 percent, respectively, for the two work levels. Several readings of less than 50 percent saturation were recorded on severe exercise. As the work level was raised, a progressive fall in arterial oxygen saturation occurred in spite of an increasing alveolar oxygen tension, and the resulting large alveolar-arterial oxygen differences can be explained by the diffusion limitations of the lung.

West, J. B. Diffusing capacity of the lung for carbon monoxide at high altitude. J. Appl. Physiol. 17:421-426(19 May 1962). Diffusing capacity of the lung for carbon monoxide (DL) was measured in London (P_B approximately 750 mm. Hg) at 15, 300 feet (4,700 meters: P_B approximately 440 mm. Hg) and at 19,000 feet (5,800 meters; P_B approximately 380 mm. Hg) on seven members of the Himalayan Scientific and Mountaineering Expedition, 1960-1961. At each altitude DL was measured at two work levels (300 and 900 Kg. -m. per minute) and at three different inspired oxygen tensions in order to separate membrane and blood components of the diffusing barrier. A steady state method was used with mixed expired gas analysis; dead space-tidal volume ratio was assumed, but calculated DL was insensitive to this ratio. There was no consistent change in DL at 15,300 feet (subjects breathing ambient air) compared with sea level, but DL was significantly increased after 7 to 10 weeks at 19,000 feet (mean changes of 15 and 19 percent for work levels of 300 and 900 Kg. -m. per minute, respectively). However, this small change in DL can be wholly accounted for by the increased rate of reactions of carbon monixide with hemoglobin due to hypoxia and by increased blood hemoglobin concentration.

West, J.B., et al. Arterial oxygen saturation during exercise at high altitude. J. Appl. Physiol. 17:617-621 (July 1962). Arterial oxygen saturations were measured on six members of the Himalayan Scientific and

Mountaineering Expedition, 1960-1961, during a wintering period at 19,000 feet (5800 meters, barometric pressure of 380 mm. Hg). The determinations were made by ear oximetry and by the analysis of venous blood from the heated hand during rest and exercise at work levels up to 1200 Kg.-m. per min. Expired gas volume and gas concentrations were also measured. The average arterial oxygen saturation at rest was 67 percent and at work levels of 300 and 900 Kg.-m. per min. was 63 and 56 percent respectively. Several readings of less than 50-percent saturation were recorded during severe exercise. The progressive fall in arterial oxygen saturation as the work level was raised occurred in spite of an increasing alveolar oxygen tension, and the resulting large alveolar-arterial oxygen differences can be explained by the diffusion limitations of the lung.

White, M.S. The effect of anoxia in high altitude flights on the electrocardiogram. Aviation Med. 11:166-180 (Dec. 1940). Four lead electrocardiograms were recorded on forty-five normal subjects exposed to anoxia through airplane flights to altitudes of 20,000 feet, with varying rates of ascent, and to an altitude of and remaining at 15,000 feet for a two-hour period. Significant changes in the electrocardiograms were noted in an early increase in rate, and a decrease in voltage of T waves (first noted at 5,000 feet and progressively becoming greater with increasing altitudes) at all levels. During a slower rate of ascent, changes were

noted which were absent in a more rapid rate of ascent. With continued flight at 15,000 feet for two hours, compensatory mechanisms were noted. With a slowing of flight speed and increasing voltage of T waves, U waves developed in slightly less than one-half the cases, becoming more prominent with increasing anoxia. All changes noted were reversed by administration of oxygen. Support is given to the theory that myocardial anoxia is a contributing factor in the production of the signs and symptoms of coronary artery disease. It is suggested that the earlier use of oxygen is indicated for all flying personnel at altitudes as low as 5000 feet in order to provide a physiologically normal individual. However, for practicability, at the present time, 7500 feet would be a minimum level above which oxygen should be required.

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Wiesinger, K., L. Perchie, and W.V. Dobel. Study on the effect of quick barometric changes without lack of oxygen. Med. Aero. (Paris) 7(4): 463-466 (1952). The origin of various physiological conditions, especially fatigue, in subjects exposed to abrupt changes of atmospheric pressure is discussed. Tests were carried out with repeated ascent to simulated altitudes of 5,000 to 10,000 meters, at a rate of ascent of 150 meters per second and descents at rates of 100 to 600 meters per second. This test on a small number of subjects showed individual differences in sensitiv · and reaction to dysbarism. Decompression or compression alone does not produce fatigue. A rate of descent not exceeding 100 meters per second is advisable in order to make equalization of external pressure and pressure in the middle ear possible.

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Wiesinger, K. On the influence of high altitude climate on several rhythms. Acta Med. Scand. Supp. 307:194-195 (1955). Measurements of the diurnal variation in the protrusion of the eyeball showed a distinct rhythm in most subjects. The globe protruded up to 0.5 millimeter more in the morning than at night. Ascent to 3475 meters altitude (Jungfraujoch) produced a slight exophthalmus and a definite damping of the diurnal rhythm in protrusion of the eyeball. An explanation may be found in a general lowering of the excitatory threshold of the nervous system. The rhythm reappears after a week's acclimatization to altitude. In addition, there was a damping of the amplitude of pupillary constriction and the diurnal temperature curve during the first week on the mountain.

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Wilbrandt, W., and B. Steinmann. Gas metabolism during ascent into higher altitudes. Arch. Ges. Physiol. 240:698-707 (1938).

Wilcox, B.R., W.C. Roberts, and E.K. Carney. The effect of reduced atmospheric oxygen concentration on closure of the ductus arteriosus in the dog. J. Surg. Res. 2(5):312-316 (Sept. 1962). In control litters, born and raised under normal circumstances, the ductus arteriosus was grossly and microscopically closed by the age of eight days. Three experimental litters were born and maintained in special chamber with an atmosphere of normal pressure but containing oxygen at a concentration of only 10 percent. Six of the 21 puppies lived 13 to 17 days and all were found to have patent ductuses on pathologic study. In dogs raised in an atmosphere of low oxygen content, anatomic closure was delayed even though internal proliferation occurred.

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Winterstein, H. Respiratory changes in mid-altitudes. Tip. Fac. Mec. (Istanbul) 15(2):505-509 (1952). A lowering of the alveolar CO_2 tension was observed in 19 out of 21 members of two excursions to

Uladag (1850 meters). The average CO_2 tension was 37.2 mm. Hg against 42 mm: Hg at sea level (difference, 11.4 percent), while the mean increase in respiratory rate amounted to only 3.9 percent. The alveolar CO_2 tensions observed were considerably lower than the calculated values. The following hypothesis was advanced: the **rarefaction** of air facilitates the diffusion of CO_2 and thereby produces a lowering of the amount and pressure of CO_2 in the blood during the ascent, thus leading to a new equilibrium at a lower concentration.

Winterstein, H. Alveolar carbon dioxide tension and altitude air. Pflueger. Arch. Ges. Physiol. 256(2):96-103 (1952). Twenty-one healthy subjects, (20 to 25 years), climbed a mountain to an altitude of 1850 meters (about 6070 feet). At this altitude, the alveolar carbon dioxide tension proved to be significantly reduced in 19 subjects (before and after ascent, 42.0 and 37.2 mm. Hg respectively; before and after descent 36.8 and 39.3 mm. Hg respectively). This reduction may be caused by a slight hypocapnia of the blood.

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Woolley, D. E. CNS excitability changes during altitude acclimatization and deacclimatization in rats. Amer. J. Physiol. 205:727-732 (Oct. 1963).

Wunsche, O. Behavior of blood lipase under influence of high altitude. Klin. Wschr. 32:584-587 (1 July, 1954).

Wunsche, O. Contributions of basic research in aviation medicine to clinical therapy. Jahrbuch der Wissenschaftlichen Gesellschaft für Luftfahrt (Braunschweig) 1954. pp. 222-225. Basic research in aviation

medicine has made important contributions to the theory and practice of medicine in general. Clinical therapy, particularly, has derived benefits from research on the mechanical and chemical effects of lowered atmospheric pressure. The compensatory reactions of the organism evoked by treatment with simulated altitude have been beneficial in bronchitis, bronchial asthma, sinusitis, anemia, and whooping cough. Experiments were conducted to clarify the non-specific responses of the organism to high altitude. Animals repeatedly exposed to altitudes of 4000 to 8000 meters showed a tendency to decreased blood albumin and continuous increase in blood gamma globulin, and a marked increase of blood lipase. The results are discussed in relation to general capacity of the organism to resist acute infections.

Wyss, S. Pulmonary edema in high mountains. Cardiologia 42(3):132-140 (1963). Two cases of acute pulmonary edema due to high altitude are reported. Failure of adaptation was observed in young subjects with normal cardiovascular systems. Within a short time, these subjects arrived from low to high altitude and immediately exerted themselves in altitudes exceeding 3000 meters. Prodromal symptoms were exhaustion, insomnia, anorexia, headache, and dyspnea of effort. Pulmonary edema is characterized by a cough, often associated with hemoptysis. In severe cases, cough is followed by loss of consciousness, coma, and, failing effective treatment, death. The condition appears to be due to a reaction to hypoxia, mainly of the vascular system, though increase in left ventricular diastolic pressure and constriction of pulmonary veins may have to be considered. With administration of oxygen, or removal to a lower altitude, the condition improves within a few hours and recovery follows in a few days. The condition may be confused with pneumonia, and the death of some mountaineers, previously attributed to fulminating pneumonia, was probably due to pulmonary edema.

Wyss, F., and A. Granoli. Changes in capillary resistance in mountain climate. Schweiz. Med. Wschr. 76:626-630 (13 July 1946).

Wyss-Dunant, E. The shock of acclimatization; observations in the Himalayas. Bull. Soc. Med. Hop. (Paris) 69(19-20):516-608 (June 1953). At 5000 to 6000 meters, the effects of altitude acclimatization prevail over the effects of low pressure. Headache, fatigue, insomnia, digestive disturbances, and nocturnal Cheyne-Stokes respiration disappear and the number of erythrocytes increases. At about 7000 meters, the lethal zone begins, where acclimatization is impossible; strong willpower alone may permit survival for 3 to 4 days, provided the caloric reserves are plentiful. With the protective equipment now available, the 8000- to 8600-meter altitude represents the limit of human endurance. Euphoric illusions induced by anoxia anesthetize the control reflexes. The subjects suffer from intense thirst, unsatiable vitamin hunger, and alkalosis.

Only men between 30 and 40 years of age should ascend to altitudes above 7500 meters. Altitude tolerance can be correlated with pulse rate; individuals whose pulse rate remains stable at altitudes up to 4000 to 5000 meters have the highest altitude tolerance.

Wyss, Dunant E. Contribution to the pathology of altitude. Rev. Prat. (Paris) 3(19):1387 (1 July 1953). Observations are made on the phenomenon of altitude acclimatization and adaptation, and the distinguishing features of each are briefly discussed. The age of the individual is reflected in the manner in which he reacts to or tolerates various altitude levels. Studies of reaction and tolerances permit the selection of individuals best suited for Alpine or Himalayan expeditions.

Y

Yamada, K., et al. Vitamin metabolism of heart muscle in anoxia. Presented at the Twenty-sixth Annual Meeting of the Japanese Circulation Society, 1962. Abstract in Jap. Circulation J. 26(11):906-907 (1962).

Yesipenko, B. Ye., and A. P. Kostromina. Uropoietic function of the kidneys under the conditions of the high mountains. AFSC N65-17823, Foreign Technology Div., Wright-Patterson AFB, Ohio. At near sea level and at altitudes of 2000 and 3200 meters, kidney function was studied in dogs that were provided with a stomach fistula and had their ureters excluded to the skin surface. The following conclusions were reached. Urine volume increased with an increase in altitude. An increase in water intake resulted in an increase in urinary volume at 2000 meters; but at higher altitudes, normalization or even a fall below normal was noted. The amount of solids increased with altitude but without forced water intake, values were lower than at near sea level. Changes in the urine formation process are the result of water equilibrium dynamics under conditions of high altitude and are directed toward aqueous homeostasis of the organism.

Yurugi, R., M. Iizuka, and T. Akiyama. On the change of gas metabolism in man during physical exercise in the low pressure environment. Jap. J. Aero Med. Psychol. 1:26-32 (Nov. 1963). Pulse rate, respiratory rate, minute volume, oxygen uptake, and carbon dioxide output were measured in four adult men before, during, and after physical exercise, hypoxia, or the two stresses combined. Hypoxia was achieved in a low-pressure chamber at a simulated altitude of 400 meters maintained for 1 hour. Physical exercise at a constant workload for 30 minutes at sea level and at simulated altitude was performed on a bicycle ergometer that was set up in the chamber. Oxygen uptake during exercise at altitude was found to be almost the same or slightly less than that at sea level, while respiratory minute volume during exercise did not increase at altitude as much as at sea level. On the contrary, heart rate during exercise increased more at altitude than at sea level. It is suggested that the compensatory hyperfunction during moderate exercise and in a mild hypoxic environment occurs mainly in the cardiovascular system by an increase in heart rate, and that the respiratory compensation is not as great as had been expected.

Z

Zach, C. Action of high mountain climate on formation of erythrocytes and hemoglobin. Riforma Med. 48: 843-845 (28 May 1932).

Zakharyan, A.B. Changes in the erythrocyte count, pulse rate and blood pressure upon an ascent to higher altitude after prior acclimatization to high altitude conditions. AFSC No65-17829, Foreign Technology Div., Wright-Patterson AFB, Ohio. Clinical and laboratory examinations were performed on young men between 20 and 26, before and after an ascent from an altitude of 3250 to 3900 meters. The subjects formed four groups that lived at the 3250-meter altitude for the following different periods of time prior to the study; 1 month, 1 to 6 months, 6 to 12 months, and over 12 months. The increase in blood pressure, pulse rate, hemoglobin content, and red blood cell count was more pronounced in the individuals who were less adapted to high altitude.

Zavala, N.B. Pulmonary circulation in the high-altitude native. An. Fac. Med. (Lima) 45:299-355 (1962). Currently, there is much speculation in bioastronautics on the long-term effects of weightlessness on cardiovascular functions during high g reentry. Certainly if the carotid sinus reflex shows adaptation to prolonged zero g, and if there is cerebral vasodilatation of a magnitude suggested by the study

related to this reflex, then any positive g exposure during reentry maneuvers might have serious consequences. It is possible also for a pilot to misinterpret a phosphene sensation during maneuvers at high positive g's as an external object, unless he is familiar with entopic effects. Respiratory function and pulmonary circulation were studied in 38 adults (age 17 to 34 years) and 32 children (age 1 to 14 years), natives and inhabitants of the Peruvian Andes (above 14,000 feet), and compared with data obtained from 25 adults living near sea level. Apart from the common clinical methods (X-ray picture of thorax, electrocardiogram, vectorcardiogram, etc.), right cardiac catheterization was employed. The principal differences observed in the altitude-acclimatized adults as compared to the lowland adults, were a moderate pulmonary hypertension, moderate increases in pulmonary vascular resistance, and in the work of the right heart. Therefore, the effects of chronic hypoxia are not comparable to those of acute hypoxia. Relations between arterioles, vasoconstriction, hypervolemia, and polycythemia are discussed, as well as the possible role of pulmonary hypertension in the high incidence of persistent ductus arteriosus at altitude.

Zharov, S.G. and A.E. Ivanov. The effects of great changes in atmospheric pressure on the human organism at high altitudes.

Voennomed. Zh. 9:61-5 (Sept. 1961). Seven healthy men were repeatedly decompressed from ground level to altitudes of 16,000 to 18,000 meters. Decompression involved pressure drops of 0.4- to 0.5-atmosphere within 1 to 1.5 seconds. A total of 52 experiments were performed. The subjects had prior training in oxygen breathing under pressure. A study was made of conditioned motor reflexes, electroencephalogram, electrocardiogram, electromyogram, abdominal muscles, changes in respiratory rate, behavior, external appearance, and subjective feelings. During the first 6 to 10 seconds there was an inhibition of conditioned reflexes and a disorder of respiratory rhythm in all subjects. EEG changes were moderate and essentially the same as during gradual ascent to altitude. Diminution of changes in respiratory functions, motor conditioned reflexes, and circulatory functions with repeated decompressions indicates the development of protective adaptation mechanisms.

Zhironkin, A. G., Increasing the resistance of animals to the toxic action of excess oxygen by acclimatization to hypoxia. AFSC N65-17806, Foreign Technology Div., Wright Patterson AFB, Ohio. Increased tolerance to the toxic effects of excess oxygen in the ambient air was successfully accomplished on small animals by subjecting them to simulated low barometric pressure equivalent to a 6000-meter altitude in a low-pressure chamber for 4 to 5 hours during 3 or 4 consecutive days. At the end of this period, the animals were subjected to a sudden change to pure oxygen under pressure of 4.5 to 6 atmospheres. These animals could withstand higher concentrations of atmospheric oxygen without toxic effects. Tissue adaptation and changes in basal metabolism could be considered the basic factors for adaptive mechanism. The same type of training could be used in cases of hypoxia.

Ziegelroth, P. Increased number of erythrocytes in mountains and icterus neonatorum. Munchen. Med. Wschr. 73:1440 (27 Aug. 1926).

Zinnitz, F., H. Koch, and W. Otto, Atmospheric disorders and disease. Z. Ges. Inn. Med 13(17):656-661 (1 Sept. 1958).

AUTHORS UNKNOWN

Alveolar air and its variation due to altitude. Med. Depor. Trab. 10:652-653 (Mar. 1947).

Hypoxia. Rev. Med. Aero. (Rio de Janeiro) 9(1-2):100-113 (Jan. -June 1957. This is a discussion of hypoxia at altitude, describing its etiology, symptoms, physiological accommodation and acute stages, preventive measures, and the use of oxygen in aviation.

Medical aspects of life at high altitudes. Proc. Roy. Soc. Med. 16:57-62 (July 1923).

Myoglobin content and enzymatic activity of human skeletal muscle - their relation with the process of adaptation to high altitude. School of Aerospace Med. N63-13342:12, Brooks AFB, Texas. Quantitative determination of myoglobin were made in the sartorius muscle of healthy human subjects, natives of sea-level and high altitude areas. The specific activity of the reduced form of diphosphopyridine nucleotide oxidase (DPNH-oxidase), DPNH- and TPNH-cytochrome c reductases, transhydrogenase and isocitric and lactic dehydrogenases were also examined. A significantly greater concentration of these elements

was found in the muscle of the high-altitude natives as compared with sea-level residents. The enzyme systems (DPNH-oxidase, TPNH-cytochrome c reductase, and transhydrogenase) similarly showed a significantly higher activity in altitude residents. It is concluded that the respiratory capacity of the muscle was apparently higher in high-altitude natives than in sea-level natives. The enhanced enzymatic activity was probably related to the higher-pigment content of the skeletal muscles. Results on myoglobin determination in several other muscles from certain sea-level patients are discussed.

Kislorodnaya Nedostatochnost, 3:610. Kiev:Izd. AN. UKR. SSR. 1963. English translation in Oxygen Insufficiency, AFSC N65-17751, Foreign Technology Div., Wright-Patterson AFB, Ohio. Collection of papers on comparative physiology of adaptation and acclimatization of the organism to high mountain climate, contemporary concepts of cell chemical mechanism in the process of adaptation to hypoxia, and other related laboratory research. For individual titles see N65-17752 through N65-17845.

Pathology of high-altitude pulmonary edema. J. A. M. A. 186:508-509 (2 Nov. 1963). Pathological findings in autopsy on two fatal cases at Cerro del Pasco, Peru (14, 300 feet above sea level) are reported in detail. Right ventricular hypertrophy and marked changes in the peripheral pulmonary arterial branches were present, both anomalies of the type found in people native to high altitude. Related preterminal arteriolar channels, directly connecting medium-and small-size pulmonary arteries with the alveolar capillaries, were also noted. There were no cardiovascular lesions to suggest cardiac insufficiency. In both cases, the cause of death was severe pulmonary edema with hyaline membranes. Further studies on the pathogenesis of high altitude pulmonary edema are needed to determine the mechanisms which lead to accumulation of edemic fluid in the pulmonary alveoli and the production of hyaline membranes.

Pulmonary edema at high altitudes (panel discussion). Med. Thorac. 19:505-22 (1962).

Resting ventilation and alveolar air on Mount Everest, with remarks on the relation of barometric pressure to altitude in mountains. J. Physiol. 135:590-610 (1957).

Science in the Himalayas. Nature 191:429-430 (1961).

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13. ABSTRACT

This bibliography was prepared from the literature surveyed as part of the study to determine the effect of altitude acclimatization on various selected stresses. This volume contains a compilation of titles and abstracts on altitude acclimatization and the exposure to chronic hypoxia. The bibliography is arranged alphabetically by last names of authors.

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