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Bibliography of Tibetan Environment & Geography

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Beall, C. M. (2000). "Oxygen saturation increases during childhood and decreases during adulthood among high altitude native Tibetans residing at 3,800-4,200m." *High Alt Med Biol* 1(1): 25-32.

This report describes age differences in oxygen saturation throughout the life cycle in a sample of high altitude native Tibetans residing in villages at 3,800-4,200 m altitude in the Tibet Autonomous Region, China. Oxygen saturation of 3,812 Tibetans was measured by pulse oximetry and a subsample of 1,582 healthy, nonpregnant, nonsmokers from 1 week to 80 years of age was selected for analyses. Infants under 1 year of age had 5-6% lower oxygen saturation than the peak of 89.8% attained at 11 years of age. There was a steady increase in mean oxygen saturation-for-age during the first decade of life, but not during the second decade. Adult males exhibited a slight decrease starting in the 20-29 year age range. Adult females maintained the peak oxygen saturation through the 40-49 year age range, exhibiting a decrease in oxygen saturation beginning in the 50-59 year age range and as a result had higher oxygen saturation than males during the female reproductive span. Thus, developmental factors during infancy and childhood, but not adolescence, enhanced oxygen transfer in this high altitude native resident Tibetan sample. The age of onset of aging processes detrimental to oxygen transfer differed for females and males.

Beall, C. M. (2000). "Tibetan and Andean contrasts in adaptation to high-altitude hypoxia." *Adv Exp Med Biol* 475: 63-74.

High-altitude environments provide natural experimental settings to investigate adaptation to environmental stress. An important evolutionary and functional question is whether sea-level human biology constrains the adaptive response. This paper presents evidence that indigenous populations of the Tibetan and Andean plateaus exhibit quantitatively different responses to hypobaric hypoxic stress. At the same altitude, Tibetan mean resting ventilation and hypoxic ventilatory response were more than one-half standard deviation higher than Andean Aymara means while Tibetan mean oxygen saturation and hemoglobin concentration were more than one standard deviation below the Andean means. Quantitative genetic analyses of the familial patterning of these traits provided indirect evidence of population differences in genes influencing them. The Tibetan and Andean patterns of oxygen transport appear equally effective functionally as evaluated by birthweight and maximal aerobic capacity across a range of altitudes.

Beall, C. M., J. Blangero, et al. (1994). "Major gene for percent of oxygen saturation of arterial hemoglobin in Tibetan highlanders." *Am J Phys Anthropol* 95(3): 271-6. This report employs a statistical genetic approach to analyze quantitative oxygen transport variables in a high-altitude (4,850-5,450 m) native Tibetan population and demonstrates the presence of a major gene influencing % O₂ saturation of arterial hemoglobin. This result suggests the hypothesis that individuals with the dominant allele for higher % O₂ saturation have a selective advantage at high altitude. Studies of the biologically distinctive Himalayan and Andean populations have greatly influenced thinking about ongoing human evolution and adaptation; this is the first statistical evidence for a major gene enhancing oxygen transport in a high-altitude native population.

Beall, C. M., G. M. Brittenham, et al. (1998). "Hemoglobin concentration of high-altitude Tibetans and Bolivian Aymara." *Am J Phys Anthropol* 106(3): 385-400. Elevated hemoglobin concentrations have been reported for high-altitude sojourners and Andean high-altitude natives since early in the 20th century. Thus, reports that have appeared since the 1970s describing relatively low hemoglobin concentration among Tibetan high-altitude natives were unexpected. These suggested a hypothesis of population differences in hematological response to high-altitude hypoxia. A case of quantitatively different responses to one environmental stress would offer an opportunity to study the broad evolutionary question of the origin of adaptations. However, many factors may confound population comparisons. The present study was designed to test the null hypothesis of no difference in mean hemoglobin concentration of Tibetan and Aymara native residents at 3,800-4,065 meters by using healthy samples that were screened for iron deficiency, abnormal hemoglobins, and thalassemias, recruited and assessed using the same techniques. The hypothesis was rejected, because Tibetan males had a significantly lower mean hemoglobin concentration of 15.6 gm/dl compared with 19.2 gm/dl for Aymara males, and Tibetan females had a mean hemoglobin concentration of 14.2 gm/dl compared with 17.8 gm/dl for Aymara females. The Tibetan hemoglobin distribution closely resembled that from a comparable, sea-level sample from the United States, whereas the Aymara distribution was shifted toward 3-4 gm/dl higher values. Genetic factors accounted for a very high proportion of the phenotypic variance in hemoglobin concentration in both samples (0.86 in the Tibetan sample and 0.87 in the Aymara sample). The presence of significant genetic variance means that there is the potential for natural selection and genetic adaptation of hemoglobin concentration in Tibetan and Aymara high-altitude populations.

Beall, C. M. and M. C. Goldstein (1987). "Hemoglobin concentration of pastoral nomads permanently resident at 4,850-5,450 meters in Tibet." *Am J Phys Anthropol* 73(4): 433-8.

This paper presents data on the hemoglobin concentration of a sample of 103 pastoral nomads who are lifelong residents of Phala, at 4,850-5,450 m, on the northern plateau of the Tibet Autonomous Region of the Peoples' Republic of China. This native population resides at the highest altitude of which we are aware and is thus exposed to the most extreme chronic hypoxic stress. However, they do not exhibit the most pronounced physiological adaptations, i.e., hemoglobin concentrations exceeding those found in all other high-altitude populations. Adult male and female mean hemoglobin concentrations of 18.2 and 16.7 gm/dl, respectively, were found. These data, in conjunction with earlier studies of ethnic Tibetans living at 3,400 m, demonstrate a pattern of increasing hemoglobin concentration (erythrocytosis) at increasing altitude of residence in the Himalayas and Tibet. At the same time, however, the hemoglobin concentration is lower than that found among Andean highlanders. These new data raise the possibility of quantitative population differences in hematological adaptation to high altitude hypoxia.

Beall, C. M., D. Laskowski, et al. (2001). "Pulmonary nitric oxide in mountain dwellers." *Nature* 414(6862): 411-2.

Beall, C. M., K. P. Strohl, et al. (1997). "Ventilation and hypoxic ventilatory response of Tibetan and Aymara high altitude natives." *Am J Phys Anthropol* 104(4): 427-47. Newcomers acclimatizing to high altitude and adult male Tibetan high altitude natives have increased ventilation relative to sea level natives at sea level. However,

Andean and Rocky Mountain high altitude natives have an intermediate level of ventilation lower than that of newcomers and Tibetan high altitude natives although generally higher than that of sea level natives at sea level. Because the reason for the relative hypoventilation of some high altitude native populations was unknown, a study was designed to describe ventilation from adolescence through old age in samples of Tibetan and Andean high altitude natives and to estimate the relative genetic and environmental influences. This paper compares resting ventilation and hypoxic ventilatory response (HVR) of 320 Tibetans 9-82 years of age and 542 Bolivian Aymara 13-94 years of age, native residents at 3,800-4,065 m. Tibetan resting ventilation was roughly 1.5 times higher and Tibetan HVR was roughly double that of Aymara. Greater duration of hypoxia (older age) was not an important source of variation in resting ventilation or HVR in either sample. That is, contrary to previous studies, neither sample acquired hypoventilation in the age ranges under study. Within populations, greater severity of hypoxia (lower percent of oxygen saturation of arterial hemoglobin) was associated with slightly higher resting ventilation among Tibetans and lower resting ventilation and HVR among Aymara women, although the associations accounted for just 2-7% of the variation. Between populations, the Tibetan sample was more hypoxic and had higher resting ventilation and HVR. Other systematic environmental contrasts did not appear to elevate Tibetan or depress Aymara ventilation. There was more intrapopulation genetic variation in these traits in the Tibetan than the Aymara sample. Thirty-five percent of the Tibetan, but none of the Aymara, resting ventilation variance was due to genetic differences among individuals. Thirty-one percent of the Tibetan HVR, but just 21% of the Aymara, HVR variance was due to genetic differences among individuals. Thus there is greater potential for evolutionary change in these traits in the Tibetans. Presently, there are two different ventilation phenotypes among high altitude natives as compared with sea level populations at sea level: lifelong sustained high resting ventilation and a moderate HVR among Tibetans in contrast with a slightly elevated resting ventilation and a low HVR among Aymara.

Beall, C. M., K. P. Strohl, et al. (1997). "Quantitative genetic analysis of arterial oxygen saturation in Tibetan highlanders." *Hum Biol* 69(5): 597-604. This study was designed to test the hypothesis that genetic differences inferred from biological kinship relationships among individuals contribute to individual variation in percentage of oxygen saturation of arterial hemoglobin (SaO₂) in a high-altitude native population. SaO₂ data were obtained by pulse oximetry from 354 nonpregnant, healthy Tibetan residents of Pen-Dri, two rural agropastoral villages at 3800-4065 m altitude in Lhasa Municipal District, Tibet Autonomous Region, China. Statistical analyses of these data from 46 pedigrees tested the hypothesis of a significant genetic contribution to SaO₂ variation. The average SaO₂ was 89.4 +/- 0.2%, with a range of 76-97%. Additive genetic effects account for 44% of the interindividual phenotypic variation in SaO₂ in the sample. Complex segregation analysis and variance decomposition analysis determined that 21% of the total phenotypic variation could be explained by a major gene influencing SaO₂. Homozygotes for the low-SaO₂ allele have a mean SaO₂ of 83.6%, whereas heterozygotes and homozygotes for the high-SaO₂ allele have means of 87.6% and 88.3%, respectively. This confirms findings in another Tibetan sample and extends the known geographic distribution of the major gene. These results suggest the hypothesis that individuals with the dominant allele for higher SaO₂ have a selective advantage in their high-altitude hypoxic environment.

Blisniuk, P., B. Hacker, et al. (2001). "Normal faulting in central Tibet since at least 13.5 Myr ago." *Nature* 412(6847): 628-32.

Bobrov, V. V. and V. M. Neronov (1995). "[The taxonomic diversity of the rodents within the limits of the Asian ecological transect]." *Izv Akad Nauk Ser Biol*(4): 462-7. The diversity of rodents is considered at various taxonomic levels within the limits of the Asian ecological transect, which crosses Asia from the Taimyr Peninsula in the north to the southern coast of Indostan and embraces territories of seven countries: Russia, Kazakhstan, Kyrgyzstan, Mongolia, China, Nepal, and India. The highest diversity of rodents is observed in the south of West Siberia and in mountains of Middle Asia. The least number of all taxa was noted in the Taimyr Peninsula and in the Tibet region.

Cao, J., Y. Zhao, et al. (2000). "[Environmental fluorine level in Tibet]." *Ying Yong Sheng Tai Xue Bao* 11(5): 777-9.

The concentration of fluorine in water, soil, fuel, food, vegetable and tea in Tibetan habitats with different environmental characteristic were measured by ion-specific electrode potentiometer. The results showed that the fluorine concentration in water, soil, fuel, food vegetable, butter tea and Zanba both of them were made from brick teas was 0.06 mg.L⁻¹, 0.45 mg.kg⁻¹, 0.10 mg.kg⁻¹, 0.06-0.33 mg.kg⁻¹, 3.09 mg.L⁻¹ and 3.61 mg.kg⁻¹, respectively. The water-soluble fluorine content in brick tea which came from Sichuan and Yunnan Provinces reached up to 533.89-617.32 mg.kg⁻¹. It is suggested that drinking brick tea may induce fluorosis in Tibetan habitats.

Cao, J., Y. Zhao, et al. (2001). "Varied ecological environment and fluorosis in Tibetan children in the nature reserve of Mount Qomolangma." *Ecotoxicol Environ Saf* 48(1): 62-5.

To determine the extent of brick tea consumption fluorosis in children living at elevations of 2000 and 4300 m, 519 children aged 8-15 years living in Xiege'er Town at 4300 m and Zhangmu Town at 2000 m were examined for dental fluorosis, their urinary fluoride concentration was determined, their dietary structure investigated, and the fluoride concentrations of various foods, freshwaters, soils, and fuels determined. Fifteen Tibetan families living in these two areas of the nature reserve of Mount Qomolangma were studied according to UNEP, FAO, and WHO guidelines for the study of dietary intake of chemical contaminants, Horowitz's classification and examination of dental fluorosis, and Dean's dental fluorosis index. The results demonstrated that dental fluorosis in Tibetan children living at an elevation of 2000 m was significantly lower than that of children at 4300 m ($P < 0.01$). Higher elevation can worsen the extent of fluorosis, leading to retention of fluoride in tissues as a result of hypoxia, but fluorosis can also be associated with the deterioration of the ecological environment at high elevation and a low-level economy. Beverages and foods mixed with brick tea water are responsible for the dental fluorosis in the children.

Cao, J., Y. Zhao, et al. (1996). "Fluorine intake of a Tibetan population." *Food Chem Toxicol* 34(8): 755-7.

Measurements of food consumption of randomly selected families and fluorine levels in food and beverages were used to calculate the fluorine intake of Tibetan people living in nomadic or semi-nomadic areas of the region and regularly consuming brick tea both as a beverage and in food. The fluorine intake of these groups (children 5.49-7.62 mg/day; adults 10.43-14.48 mg/day) was much higher than that of members of a Han population living in the region (children 1.44 mg/day; adults 2.54 mg/day). The amounts of fluorine consumed by the Tibetan inhabitants are at least twice the WHO suggested limit (2 mg/day). Tea plants are rich in fluorine, and the

highest levels are found in older leaves which are used to make brick tea. We conclude that brick tea is the major source of fluorine intake by the Tibetan population studied.

Chasseur, C., C. Suetens, et al. (2001). "A 4-year study of the mycological aspects of Kashin-Beck disease in Tibet." *Int Orthop* 25(3): 154-8.

In order to clarify the association between mycotoxin-producing fungi in food and Kashin-Beck disease (KBD), we examined the occurrence and contamination levels of fungi in samples of barley grain, from KBD-affected families and from unaffected families in endemic areas. A control area without the occurrence of KBD served as reference. The first results obtained in 1995 showed that total mesophilic fungal contamination of barley grain was consistently higher in families with KBD.

Trichothecium roseum (Pers) Link ex gray, *Dreschlera* Ito and *Alternaria* Nees ex Fr. were the three most common fungi significantly associated with KBD. In 1996 we again observed a significant difference between affected and non-affected families, especially with *Trichothecium roseum* and *Ulocladium* Preuss. On this basis, measures to prevent KBD were suggested and a preventive program has been set up since 1998 in 20 new villages.

Chen, Q. H., R. L. Ge, et al. (1997). "Exercise performance of Tibetan and Han adolescents at altitudes of 3,417 and 4,300 m." *J Appl Physiol* 83(2): 661-7.

The difference was studied between O₂ transport in lifelong Tibetan adolescents and in newcomer Han adolescents acclimatized to high altitude. We measured minute ventilation, maximal O₂ uptake, maximal cardiac output, and arterial O₂ saturation during maximal exercise, using the incremental exercise technique, at altitudes of 3,417 and 4,300 m. The groups were well matched for age, height, and nutritional status. The Tibetans had been living at the altitudes for a longer period than the Hans (14.5 +/- 0.2 vs. 7.8 +/- 0.8 yr at 3,417 m, P < 0.01; and 14.7 +/- 0.3 vs. 5.3 +/- 0.7 yr at 4,300 m, P < 0.01, respectively). At rest, Tibetans had significantly greater vital capacity and maximal voluntary ventilation than the Hans at both altitudes. At maximal exercise, Tibetans compared with Hans had higher maximal O₂ uptake (42.2 +/- 1.7 vs. 36.7 +/- 1.2 ml . min⁻¹ . kg⁻¹ at 3,417 m, P < 0.01; and 36.8 +/- 1.9 vs. 30.0 +/- 1.4 ml . min⁻¹ . kg⁻¹ at 4,300 m, P < 0.01, respectively) and greater maximal cardiac output (12.8 +/- 0.3 vs. 11.4 +/- 0.2 l/min at 3,417 m, P < 0.01; 11.5 +/- 0.5 vs. 10.0 +/- 0.5 l/min at 4,300 m, P < 0.05, respectively). Although the differences in arterial O₂ saturation between Tibetans and Hans were not significant at rest and during mild exercise, the differences became greater with increases in exercise workload at both altitudes. We concluded that exposure to high altitude from birth to adolescence resulted in an efficient O₂ transport and a greater aerobic exercise performance that may reflect a successful adaptation to life at high altitude.

Cheng, T. O. (1989). "Heart disease in Tibet." *Lancet* 2(8655): 163.

Curran, L. S., J. Zhuang, et al. (1995). "Hypoxic ventilatory responses in Tibetan residents of 4400 m compared with 3658 m." *Respir Physiol* 100(3): 223-30.

Lifelong Tibetan residents of 3658 m ventilate as much and have hypoxic and hypercapnic ventilatory responsiveness as least as great as acclimatized newcomers, and likely greater than lifelong North or South American high-altitude residents. To determine whether Tibetans residing at altitudes > 3658 m maintained similar levels of ventilation, hypoxic and hypercapnic ventilatory responses, we transported 20 lifelong residents of > or = 4400 m to 3658 m for comparison with 27 similarly-aged male Tibetan residents of 3658 m. At 3658 m, the 4400 m compared with the 3658

m Tibetans had similar levels of minute ventilation and arterial O₂ saturation, higher respiratory quotients but lower hypoxic ventilatory responses. We conclude that Tibetan residents of > or = 4400 m ventilate as much as Tibetan residents of 3658 m despite an altitude-associated blunting of their hypoxic ventilatory responses. Thus, factors other than hypoxic ventilatory chemosensitivity are likely to be important contributors to resting ventilation among Tibetan high altitude residents.

Curran, L. S., J. Zhuang, et al. (1998). "Superior exercise performance in lifelong Tibetan residents of 4,400 m compared with Tibetan residents of 3,658 m." *Am J Phys Anthropol* 105(1): 21-31.

Few environments challenge human populations more than high altitude, since the accompanying low oxygen pressures (hypoxia) are pervasive and impervious to cultural modification. Work capacity is an important factor in a population's ability to thrive in such an environment. The performance of work or exercise is a measure of the integrated functioning of the O₂ transport system, with maximal O₂ uptake ($\dot{V}O_{2max}$) a convenient index of that function. Hypoxia limits the ability to transport oxygen: maximal O₂ uptake decreases with ascent to high altitude, and years of high altitude residence do not restore sea level $\dot{V}O_{2max}$ values. Since Tibetans live and work at some of the highest altitudes in the world, their ability to exercise at very high altitude (>4,000 m) may define the limits of human adaptation to hypoxia. We transported 20 Tibetan lifelong residents of > or = 4,400 m down to 3,658 m in order to compare them with 16 previously studied Tibetan residents of Lhasa (3,658 m). The two groups of Tibetans were matched for age, weight, and height. All studies were performed in Lhasa within 3 days of the 4,400 m Tibetans' arrival. Standard test protocol and criteria were used for attaining $\dot{V}O_{2max}$ on a Monark bicycle ergometer, while measuring oxygen uptake ($\dot{V}O_2$, ml/kg - min STPD), heart rate (bpm), minute ventilation (VE, l/min BTPS), and arterial oxygen saturation (SaO₂, %). The 4,400 m compared with 3,658 m residents had, at maximal effort, similar $\dot{V}O_2$ (48.5 +/- 1.2 vs. 51.2 +/- 1.4 ml/kg - min, P = NS), higher workload attained (211 +/- 6 vs. 177 +/- 7 watts, P < 0.01), lower heart rate (176 +/- 2 vs. 191 +/- 2 bpm, P < 0.01), lower ventilation (127 +/- 5 vs. 149 +/- 5 l/min BTPS, P < 0.01), and similar SaO₂ (81.9 +/- 1.0 vs. 83.7 +/- 1.2%, P = NS). Furthermore, over the range of submaximal workloads, 4,400 m compared with 3,658 m Tibetans had lower $\dot{V}O_2$ (P < 0.01), lower heart rates (P < 0.01), and lower ventilation (P < 0.01) and SaO₂ (P < 0.05). We conclude that Tibetans living at 4,400 m compared with those residing at 3,658 m achieve greater work performance for a given $\dot{V}O_2$ at submaximal and maximal workloads with less cardiorespiratory effort.

Curran, L. S., J. Zhuang, et al. (1997). "Ventilation and hypoxic ventilatory responsiveness in Chinese-Tibetan residents at 3,658 m." *J Appl Physiol* 83(6): 2098-104.

When breathing ambient air at rest at 3,658 m altitude, Tibetan lifelong residents of 3,658 m ventilate as much as newcomers acclimatized to high altitude; they also ventilate more and have greater hypoxic ventilatory responses (HVRs) than do Han ("Chinese") long-term residents at 3,658 m. This suggests that Tibetan ancestry is advantageous in protecting resting ventilation levels during years of hypoxic exposure and is of interest in light of the permissive role of hypoventilation in the development of chronic mountain sickness, which is nearly absent among Tibetans. The existence of individuals with mixed Tibetan-Chinese ancestry (Han-Tibetans) residing at 3,658 m affords an opportunity to test this hypothesis. Eighteen men born in Lhasa, Tibet, China (3,658 m) to Tibetan mothers and Han fathers were compared with 27 Tibetan men and 30 Han men residing at 3,658 m who were previously studied. We used the same study procedures (minute ventilation was

measured with a dry-gas flowmeter during room air breathing and hyperoxia and with a 13-liter spirometer-rebreathing system during the hypoxic and hypercapnic tests). During room air breathing at 3,658 m (inspired O₂ pressure = 93 Torr), Han-Tibetans resembled Tibetans in ventilation (12.1 +/- 0.6 vs. 11.5 +/- 0.5 l/min BTPS, respectively) but had HVR that were blunted (63 +/- 16 vs. 121 +/- 13, respectively, for HVR shape parameter A) and declined with increasing duration of high-altitude residence. During administered hyperoxia (inspired O₂ pressure = 310 Torr) at 3,658 m, the paradoxical hyperventilation previously seen in Tibetan but not Han residents at 3,658 m (11.8 +/- 0.5 vs. 10.1 +/- 0.5 l/min BTPS) was absent in these Han-Tibetans (9.8 +/- 0.6 l/min BTPS). Thus, although longer duration of high-altitude residence appears to progressively blunt HVR among Han-Tibetans born and residing at 3,658 m, their Tibetan ancestry appears protective in their maintenance of high resting ventilation levels despite diminished chemosensitivity.

Cyranoski, D. (2002). "Microbe hunt raises doubts over local benefits of bioprospecting." *Nature* 420(6912): 109.

Droma, T., R. G. McCullough, et al. (1991). "Increased vital and total lung capacities in Tibetan compared to Han residents of Lhasa (3,658 m)." *Am J Phys Anthropol* 86(3): 341-51.

Larger chest dimensions and lung volumes have been reported for Andean high-altitude natives compared with sea-level residents and implicated in raising lung diffusing capacity. Studies conducted in Nepal suggested that lifelong Himalayan residents did not have enlarged chest dimensions. To determine if high-altitude Himalayans (Tibetans) had larger lung volumes than acclimatized newcomers (Han "Chinese"), we studied 38 Tibetan and 43 Han residents of Lhasa, Tibet Autonomous Region, China (elevation 3,658 m) matched for age, height, weight, and smoking history. The Tibetan compared with the Han subjects had a larger total lung capacity [6.80 +/- 0.19 (mean +/- SEM) vs 6.24 +/- 0.18 l BTPS, P less than 0.05], vital capacity (5.00 +/- 0.08 vs 4.51 +/- 0.10 l BTPS, P less than 0.05), and tended to have a greater residual volume (1.86 +/- 0.12 vs 1.56 +/- 0.09 l BTPS, P less than 0.06). Chest circumference was greater in the Tibetan than the Han subjects (85 +/- 1 vs 82 +/- 1 cm, P less than 0.05) and correlated with vital capacity in each group as well as in the two groups combined ($r = 0.69$, P less than 0.05). Han who had migrated to high altitude as children (less than or equal to 5 years old, $n = 6$) compared to Han adult migrants (greater than or equal to 18 years old, $n = 26$) were shorter but had similar lung volumes and capacities when normalized for body size. The Tibetans' vital capacity and total lung capacity in relation to body size were similar to values reported previously for lifelong residents of high altitude in South and North America. Thus, Tibetans, like North and South American high-altitude residents, have larger lung volumes. This may be important for raising lung diffusing capacity and preserving arterial oxygen saturation during exercise.

Duff, J. (1999). "The "Tibetan tuck": a dry land-cold conditions survival position equivalent to that used in cold water." *Wilderness Environ Med* 10(3): 206-7.

Ge, R. L., Q. H. Chen, et al. (1994). "Higher exercise performance and lower VO₂max in Tibetan than Han residents at 4,700 m altitude." *J Appl Physiol* 77(2): 684-91.

To examine the hypothesis that the pathway of adaptation to high altitude in natives differs considerably from that in newcomers, we measured maximal O₂ uptake (VO₂max), minute ventilation, anaerobic threshold (AT), blood lactate, and blood gases during maximal exercise in 17 lifelong Tibetan residents and 14 acclimatized

Han Chinese newcomers living at the altitude of 4,700 m. The two groups were similar in age, height, and weight, and the subjects were nonathletes. Although VO₂max was significantly lower in the Tibetans than in the Hans (30.4 +/- 1.5 vs. 36.0 +/- 1.9 ml.min⁻¹.kg⁻¹ STPD; P < 0.05), at maximal exercise effort the exercise workload was greater (167.7 +/- 4.2 vs. 150.0 +/- 5.9 W; P < 0.05). The mean AT values (in % VO₂max) in the Tibetan and Han subjects were 84.1 and 61.6%, respectively (P < 0.01). Minute ventilation at maximal exercise was significantly lower in the Tibetans than in the Hans (68.4 +/- 3.4 vs. 79.7 +/- 4.1 l/min BTPS; P < 0.05), whereas heart rate at maximal effort was equivalent in the two groups. The Tibetans showed lower blood lactate value than did the Hans both before and at the end of exercise. We conclude that the Tibetan natives have higher exercise performance and AT but lower VO₂max and blood lactate concentration than do acclimatized Han newcomers. These results may reflect the effects of genetic or peripheral adaptation factors in the Tibetan natives.

Gibson, C. (2000). "Six weeks in Tibet." *Nurs Times* 96(41): 50.

Guan, G., H. Yin, et al. (2002). "Transmission of *Babesia* sp to sheep with field-collected *Haemaphysalis qinghaiensis*." *Parasitol Res* 88(13): S22-4. *Haemaphysalis qinghaiensis* ticks collected in the Gannan Tibet Autonomous Region were infested onto a sheep from a *Babesia*-free area. A strain of small *Babesia* (1.8-2.1 microm in length) was isolated from the sheep. Most of the *Babesia* in erythrocytes were round, oval, single pyriform, double pyriform, budding or elongated in form. Measurements were made of 100 single sides of the double-pyriform *Babesia* and compared with those for *B. motasi* and *B. ovis* from Holland, using Student's t-test. The Gannan small *Babesia* was similar to the *B. ovis* from Holland, but differed significantly from the Dutch *B. motasi*.

Guo, S., Z. Yuan, et al. (2002). "Epidemiology of ovine theileriosis in Ganan region, Gansu Province, China." *Parasitol Res* 88(13 Suppl 1): S36-7. The epidemiology of ovine theileriosis in Gannan Tibet Autonomous Region was investigated. The results of these studies indicate that this disease is endemic in the following counties of Gannan where the vector tick was identified as *Haemaphysalis qinghaiensis*: Luqu, Xiahe, Hezuo, Zhuoni, Lintan, Diebu, Maqu. The disease mainly occurred from March to May and some cases also occurred in September and October. The incidence rates in lambs of sheep brought from areas free of the disease were high. On average, the incidence and mortality rates were 60.8% and 81.5% respectively. In adult sheep, the incidence and mortality rates were 17.12% and 65.78% respectively. The mean incidence rate of young goats was 40% and the mortality was 85.71%. The incidence rate for adult goats was 8.06% and the mortality was 73.33%. During the carrier period, the infection rates of lambs, young goats, adult sheep and adult goats were 91.7%, 64.29%, 63.13%, and 20% respectively.

Halperin, B. D., S. Sun, et al. (1998). "ECG observations in Tibetan and Han residents of Lhasa." *J Electrocardiol* 31(3): 237-43. In order to compare the prevalence of electrocardiographic (ECG) abnormalities suggestive of right ventricular hypertrophy in native and immigrant populations residing at high altitude, a retrospective review was undertaken of data obtained from a random survey of healthy volunteers and persons with chronic mountain sickness (CMS). All persons included in the survey were ambulatory volunteers from the general community who were evaluated at the Tibet Institute of Medical Science in Lhasa, where the elevation is 3,658 meters. The 74 residents of Lhasa, whose

ECGs were studied, included 30 healthy Tibetan natives of Lhasa; 24 healthy Han (Chinese) immigrants, born at or near sea level, who had migrated to high altitude as children or adults; and 20 persons with symptoms of CMS. The ECGs of all subjects were reviewed for predetermined criteria suggestive of right ventricular hypertrophy, which were found to be present in 17% of healthy Tibetan natives, 29% of healthy Han immigrants, and 50% of CMS patients. The Han subjects who had migrated as children presented evidence of right ventricular hypertrophy more commonly than did adult immigrants. The overwhelming majority (90%) of persons with CMS were Han. Thus, the frequency of ECG abnormalities consistent with right ventricular hypertrophy was similar in healthy young Tibetan and Han men, but these abnormalities were less common in Tibetan natives than in Han who had migrated to high altitude as children or in CMS patients. The prevalence of ECG evidence of right ventricular hypertrophy increased with duration of high altitude residence among Han.

Harris, N. S., P. B. Crawford, et al. (2001). "Nutritional and health status of Tibetan children living at high altitudes." *N Engl J Med* 344(5): 341-7.

BACKGROUND: Children living at high altitudes often have delayed growth, but whether growth retardation is related to altitude or to other factors is not known. **METHODS:** A multicultural health care team assessed 2078 Tibetan children 0 to 84 months of age for anthropometric and clinical signs of malnutrition. The children lived in 11 counties, which contained more than 50 diverse urban and nonurban (nomadic, agricultural, or periurban) communities in the Tibet Autonomous Region of China. The height and weight of the children were compared with those of U.S. children. Height and weight were expressed as z scores (the number of standard deviations from the median of the age- and sex-specific reference group). **RESULTS:** The mean z score for height fell from -0.5 to -1.6 in the first 12 months of life and generally ranged from -2.0 to -2.4 in older children. Overall, of 2078 children, 1067 (51 percent) had moderately or severely stunted growth, as defined by a z score of -2.0 or lower. Of the 1556 children 24 months of age or older, 871 (56 percent) had stunted growth, which was severe (z score, -3.0 or lower) in 380 (24 percent). Among the children in this age group, 787 of the 1313 nonurban children (60 percent) had stunting, as compared with 84 of the 243 urban children (35 percent). Stunting was associated with clinical conditions such as rickets, abdominal distention, hair depigmentation, and skin lesions and with a maternal history of hepatitis or goiter. Stunting was not associated with altitude, after adjustment for the type of community. **CONCLUSIONS:** In Tibetan children, severe stunting due to malnutrition occurs early in life, and morbidity is high.

Heath, D. (1989). "Missing link from Tibet." *Thorax* 44(12): 981-3.

Hoppeler, H. and M. Vogt (2001). "Muscle tissue adaptations to hypoxia." *J Exp Biol* 204(Pt 18): 3133-9.

This review reports on the effects of hypoxia on human skeletal muscle tissue. It was hypothesized in early reports that chronic hypoxia, as the main physiological stress during exposure to altitude, per se might positively affect muscle oxidative capacity and capillarity. However, it is now established that sustained exposure to severe hypoxia has detrimental effects on muscle structure. Short-term effects on skeletal muscle structure can readily be observed after 2 months of acute exposure of lowlanders to severe hypoxia, e.g. during typical mountaineering expeditions to the Himalayas. The full range of phenotypic malleability of muscle tissue is demonstrated in people living permanently at high altitude (e.g. at La Paz, 3600-4000 m). In addition, there is some evidence for genetic adaptations to hypoxia in high-altitude

populations such as Tibetans and Quechuas, who have been exposed to altitudes in excess of 3500 m for thousands of generations. The hallmark of muscle adaptation to hypoxia in all these cases is a decrease in muscle oxidative capacity concomitant with a decrease in aerobic work capacity. It is thought that local tissue hypoxia is an important adaptive stress for muscle tissue in exercise training, so these results seem contra-intuitive. Studies have therefore been conducted in which subjects were exposed to hypoxia only during exercise sessions. In this situation, the potentially negative effects of permanent hypoxic exposure and other confounding variables related to exposure to high altitude could be avoided. Training in hypoxia results, at the molecular level, in an upregulation of the regulatory subunit of hypoxia-inducible factor-1 (HIF-1). Possibly as a consequence of this upregulation of HIF-1, the levels mRNAs for myoglobin, for vascular endothelial growth factor and for glycolytic enzymes, such as phosphofructokinase, together with mitochondrial and capillary densities, increased in a hypoxia-dependent manner. Functional analyses revealed positive effects on V(O₂)max (when measured at altitude) on maximal power output and on lean body mass. In addition to the positive effects of hypoxia training on athletic performance, there is some recent indication that hypoxia training has a positive effect on the risk factors for cardiovascular disease.

Hu, T. S. and Y. X. Lao (1987). "An epidemiologic survey of senile cataract in China." *Dev Ophthalmol* 15: 42-51.

This paper is based on data obtained in blindness screening in 7 rural areas throughout China and presented at the Second National Conference of the Chinese Ophthalmologic Society in 1979. This comparative study of the incidence of senile cataract in relation to geographic and meteorologic factors, with special reference to solar radiation, indicates that cataract incidence increases with decrease in latitude or increase in altitude due to increased solar radiation. Zedang in Tibet, with the highest altitude and low latitude (29 degrees N) has the highest incidence (1.32%) of the areas surveyed, followed by Aleitai 0.25% and Zhongshan (0.23%), whereas the incidences in lowland areas are between 0.12 and 0.14%, the lowest surveyed being in Zhongmou (0.066%). The differences in cataract incidence are apparently associated with solar radiation. Yu and coworkers in their research demonstrated the evidence for the solar UV-induced lowering of sulfhydryl level in the Tibet human lens nucleus. Therefore, these findings furnish some evidence supporting the theory that sunlight enhances cataract formation.

Huang, S. Y., S. Sun, et al. (1992). "Internal carotid arterial flow velocity during exercise in Tibetan and Han residents of Lhasa (3,658 m)." *J Appl Physiol* 73(6): 2638-42.

Cerebral blood flow increases with acute exposure to high altitude, but the effect of hypoxia on the cerebral circulation at rest and during exercise appears influenced by the duration of high-altitude exposure. To determine whether internal carotid artery flow velocity increased with exercise in long-term residents of high altitude and whether resting values and the response to exercise differed in lifelong vs. acclimatized newcomer male residents of high altitude, we studied 15 native Tibetan and 11 Han ("Chinese") 6 +/- 2-yr residents of Lhasa (3,658 m), Tibet Autonomous Region, China. Noninvasive Doppler ultrasound was used to measure internal carotid artery diameter, mean flow velocity, and, in combination, hemoglobin and arterial O₂ saturation to assess cerebral O₂ delivery. Tibetan and Han groups were similar in body size and resting internal carotid artery diameter, blood pressure, hemoglobin concentration, internal carotid artery mean flow velocity, and calculated cerebral O₂ delivery. Submaximal exercise increased internal carotid artery mean flow velocity and cerebral O₂ delivery in the Tibetan and Han subjects. At peak exercise, the

Tibetans sustained the increase in flow velocity and cerebral O₂ delivery, whereas the Hans did not. Across all exercise levels up to and including peak effort, the Tibetans demonstrated a greater increase in internal carotid artery flow velocity and cerebral O₂ delivery relative to resting values than did the Hans. The greater cerebral O₂ delivery was accompanied by increased peak exercise capacity in the Tibetan compared with the Han group. Our findings suggest that the cerebral blood flow response to exercise is maintained in Tibetan lifelong residents of high altitude.

Iwamoto, T., I. Kuwahira, et al. (2002). "[Evaluation of cardiopulmonary function in Japanese Himalayan climbers to the Himalayas underin a hypobaric hypoxic chamber]." *Nihon Kokyuki Gakkai Zasshi* 40(4): 287-91.

The Tokai University and Tibet University Scientific Friendship Expedition 2001 succeeded in reaching the summit of Kula Kangri (7,538 m) in the Himalayas without supplementary O₂ in May, 2001. Before this expedition, the cardiopulmonary function of all members was evaluated using a hypobaric hypoxic chamber in which the barometric pressure was gradually lowered to a simulated altitude of 6000 m. Whenever a member's PaO₂ was lower than 40 torr during the experiment, supplementary O₂ was given. The results were divided into two groups, Group A and Group B, according to whether supplementary O₂ was used. Group A subjects did not need O₂ even at an altitude of 6,000 m, whereas Group B subjects did when they reached an altitude of 5,000 m. Seven the eight Group A members had climbed mountains over 4,000 m several times, whereas twelve out of the thirteen members of Group B had no mountaineering experience. The mean PaO₂ and PaCO₂ of Group A at 6000 m were 41.9 torr and 31.9 torr, respectively, while those of Group B at 5000 m were 35.8 torr and 35.9 torr. There was a significant difference in the degree of hyperventilation between Group A and Group B. No difference was observed between the two groups in systolic and diastolic arterial blood pressure, but the heart rate in Group B increased significantly under hypoxia. These results suggest that the experience of climbing mountains over 4000 m may lead to significant differences in cardiopulmonary function under hypoxia.

Jacobs, A., B. Keymeulen, et al. (1993). "Semiquantitative analysis of cerebral blood flow by means of ⁹⁹Tcm-HMPAO SPECT in individuals before and after a high altitude Himalayan expedition." *Nucl Med Commun* 14(8): 702-5.

Nine members of the 'Belgian Tibet Expedition 1991' underwent a ⁹⁹Tcm-hexamethylpropyleneamine oxime (HMPAO) brain single photon emission computed tomographic study before and after their stay at high altitude. Cerebral and cerebellar activity were analysed in three circumference profiles, representing the lower, middle and upper transaxial sections of the brain. The count value of each volume element (VE) was normalized to the maximum cerebellar value. In order to compare individual regional cerebral blood flow (rCBF) before and after the expedition, the relative differences in rCBF were calculated for each VE as: $\text{rel delta (\%)} = 100 \times (\text{value after expedition} - \text{value before expedition}) / \text{value before expedition}$. In 4/9 cases regional rel delta values were negative in most cortical regions; in 3/9 individuals nonsignificant changes were found and 2/9 climbers showed a positive rel delta value in most cortical regions. For the group as a whole there was (1) a mean decrease of 1.7% in global cortical CBF and (2) a significantly ($P < 0.01$) diminished rCBF was observed in both temporal and the left frontotemporal areas.

Javitt, J. C. and H. R. Taylor (1994). "Cataract and latitude." *Doc Ophthalmol* 88(3-4): 307-25.

For many years, it has been suggested that exposure to sunlight, particularly its ultraviolet component, may be associated with an increased risk of senile cataract. This paper addresses 1) the physical and geographic variables that affect the entry of ultraviolet light in the eye; 2) the epidemiologic evidence that associates cataract with ultraviolet light exposure; and 3) the effectiveness of personal barrier protection (i.e. sunglasses and hats) in reducing ocular exposure to ultraviolet light. The epidemiologic evidence is drawn from studies in Australia, China, Tibet, and the United States. The U.S. evidence consists of data from the Maryland Watermen study and analyses of cataract surgery under the Medicare program which provides health insurance for nearly all Americans age 65 and over (30 million) and pays for 85% of the 1.3 million cataract extractions performed annually in the U.S. Analysis of the Medicaid data shown that, after controlling for age, sex, and race, and income of the population and also controlling for supply of ophthalmologists, optometrists, price of surgery and local practice costs, the strongest predictor of cataract surgery likelihood in a Medicare beneficiary is the person's latitude of residence. Latitude correlates directly with the UV-B content of sunlight, because the incident angle of the sun determines the atmospheric penetration of ultraviolet radiation. Data suggest that the probability of cataract surgery in the U.S. increases by 3% for each 1 degree decrease (i.e. more Southerly) in latitude.

Jensen, R. H., S. Zhang, et al. (1997). "Glycophorin A somatic cell mutation frequencies in residents of Tibet at high altitudes." *Health Phys* 73(4): 663-7. Since cosmic radiation is absorbed by the atmosphere surrounding the Earth, people who live at high altitude receive significantly larger amounts of cosmic radiation exposure than do those who live at low altitude. The glycophorin A-based somatic mutation assay was performed on 36 blood samples from two populations of Tibet inhabitants to determine whether residents at high altitude (4,300 m) accumulate more somatic mutations than do those who live at low altitude (1,500-1,900 m). These two populations differ in estimated cumulative lifetime cosmic radiation dose, with high altitude residents having received a mean of 111 mSv while low altitude residents received a mean of 27 mSv. Results showed no significant difference in peripheral blood variant erythrocyte frequency between these two populations and no difference from results of a previous study on Finnish workers who live at very low altitude (<500 m).

Joshi, B. R., L. M. Gibbons, et al. (1997). "Ostertagia nianqingtanggulaensis Kung & Li, 1965 (Nematoda: Trichostrongyloidea) from sheep and goats at high altitudes in Nepal." *J Helminthol* 71(1): 21-7. The trichostrongyloid nematode *Ostertagia nianqingtanggulaensis* Kung & Li, 1965, previously recorded only from sheep in Tibet, is redescribed and is shown to be a common parasite of both sheep and goats at higher altitudes in the Himalayan foothills of western Nepal. Herbage examination indicated that infective larvae can overwinter on snow covered slopes. Use of tracer animals confirmed that migratory flocks are exposed to infection when grazing on alpine pastures during the summer months. In contrast, nearby non-migratory flocks kept at lower altitudes did not harbour *O. nianqingtanggulaensis* and tracer animals grazed with these flocks did not become infected with this species.

Kayser, B. (1996). "Lactate during exercise at high altitude." *Eur J Appl Physiol Occup Physiol* 74(3): 195-205. In acclimatized humans at high altitude the reduction, compared to acute hypoxia, of the blood lactate concentration (l_a) at any absolute oxygen uptake (VO_2), as well as the reduction of maximum l_a (l_{amax}) after exhaustive exercise, compared to both

acute hypoxia or normoxia, have been considered paradoxical, and these phenomena have therefore become known as the "lactate paradox". Since, at any given power output and VO_2 , mass oxygen transport to the contracting locomotor muscles is not altered by the process of acclimatization to high altitude, the gradual reduction in $[\text{La-}]_{\text{max}}$ in lowlanders exposed to chronic hypoxia seems not to be due to changes in oxygen availability at the tissue level. At present, it appears that the acclimatization-induced changes in $[\text{La-}]$ during exercise are the result of at least two mechanisms: (1) a decrease in maximum substrate flux through aerobic glycolysis due to the reduced $\text{VO}_{2\text{max}}$ in hypoxia; and (2) alterations in the metabolic control of glycogenolysis and glycolysis at the cellular level, largely because of the changes in adrenergic drive of glycogenolysis that ensue during acclimatization, although effects of changes in peripheral oxygen transfer and the cellular redox state cannot be ruled out. With regard to the differences in lactate accumulation during exercise that have been reported to occur between lowlanders and highlanders, both groups either being acclimatized or not, these do not seem to be based upon fundamentally different metabolic features. Instead, they seem merely to reflect points along the same continuum of phenotypic adaptation of which the location depends on the time spent at high altitude.

Kayser, B., H. Hoppeler, et al. (1996). "Muscle ultrastructure and biochemistry of lowland Tibetans." *J Appl Physiol* 81(1): 419-25.

Muscle ultrastructure and biochemistry in vastus lateralis muscle biopsies and the response to exercise of 8 lowland Tibetans (T) were compared with those of 8 Nepalese lowlanders (N). Blood hemoglobin was lower in T than in N (119 ± 3 vs. 131 ± 2 g/l; $P < 0.05$). Peak O_2 consumption per kilogram of body mass was similar [37.9 ± 2.2 (T) vs. 40.1 ± 1.36 ml.min⁻¹.kg body mass⁻¹ (N)]. Maximum exercise blood lactate was the same [11.4 (T) ± 0.5 vs. 11.3 ± 0.6 mM (N)]. Muscle fiber type distribution was similar [type I, 58.6 ± 3.4 (N) vs. $57.0 \pm 3.4\%$ (T); type IIa, 24.1 ± 3.5 vs. $27.1 \pm 1.6\%$; type IIb, 17.4 ± 1.4 vs. $15.9 \pm 2.9\%$]. T had smaller fiber cross-sectional areas [$3,413 \pm 677$ (T) vs. $3,895 \pm 447$ microns² (N); $P < 0.05$] but had similar number of capillaries per muscle fiber [1.35 ± 0.23 (T) vs. 1.46 ± 0.08 (N)] and muscle fiber area supplied per capillary [399 ± 29 (T) vs. 382 ± 65 mm² (N)]. Total mitochondrial volume density was much lower in T ($3.99 \pm 0.17\%$) than in N ($5.51 \pm 0.19\%$) ($P < 0.025$). Mirroring mitochondrial volume density, citrate synthase and 3-hydroxyacyl-CoA dehydrogenase activities were lower in T than in N ($P < 0.05$). The activities of L-lactate dehydrogenase and hexokinase were the same in both groups. T had significantly less muscle fiber lipid droplets than did N, which correlated with the low activity of 3-hydroxyacyl-CoA dehydrogenase ($r = 0.57$, $P = 0.02$). In conclusion, lowland-born T have a low mitochondrial volume-to-specific peak O_2 consumption ratio, which, based on previous measurements on altitude-born Sherpas (B. Kayser, H. Hoppeler, H. Claassen and P. Cerretelli. *J. Appl. Physiol.* 70: 1938-1942, 1991), appears to be an inborn feature.

Kayser, B., C. Marconi, et al. (1994). "The metabolic and ventilatory response to exercise in Tibetans born at low altitude." *Respir Physiol* 98(1): 15-26.

The exercise response of 20 Tibetans (T) born and living in Kathmandu, Nepal (1300 m) was compared to that of 21 age- and sex-matched local lowlanders. The subjects carried out an incremental exercise protocol on a bicycle ergometer (30 watt steps every 4 min) until exhaustion. The kinetics of readjustment of VO_2 measured as half time (t_{on}) upon a 90 watt constant load exercise was also determined. Breath-by-breath gas exchange, heart rate (HR) and blood lactate concentration ($[\text{La}]$) were measured at rest, at the end of each load and during recovery. The slope of the

straight line relating VO_2 to work load was $10.8 \text{ ml.watt}^{-1}$ in both groups which corresponds to a mechanical efficiency of 0.26 (assuming a RQ of 0.89 and an energy equivalent of $20.9 \text{ kJ.L}^{-1} \text{ O}_2$). At submaximal loads T were characterized by higher VE ($P < 0.05$), $\text{VE} \cdot \text{VO}_2^{-1}$ ($P < 0.01$) and VCO_2 levels ($P < 0.001$) than N. The found higher VE in T, resulting from a lower tidal volume coupled to a higher respiratory frequency, led to higher PETO_2 ($P < 0.001$) and SaO_2 ($P < 0.001$) at all work levels. Absolute $\text{VO}_{2\text{max}}$ in the two investigated groups were 1977 ± 72 (T) and 2095 ± 80 (N) ml.min^{-1} (NS). Specific (i.e. per kg body weight) $\text{VO}_{2\text{max}}$ were identical (37.0 ± 1.1 [T] vs. $36.7 \pm 1.1 \text{ ml.kg}^{-1} \cdot \text{min}^{-1}$ [N]). $[\text{La}]_{\text{max}}$ were 11.4 ± 0.4 (T) vs. 12.3 ± 0.4 (N) mM (NS). $[\text{La}]$ accumulation in blood as a function of workload and its rate of disappearance during recovery were similar. t-on at 90 watt was 30.7 ± 2.4 sec in T and 28.9 ± 2.3 sec in N (NS). The corresponding average contracted O_2 deficit were 971 ml for T and 994 ml for N (NS). In conclusion, Tibetans born at low altitude do not seem to differ from lowlanders with regard to their metabolic response whereas their ventilatory response to exercise is greater.

Kleinsasser, A. and A. Loeckinger (2002). "Brief report: pressure support ventilation during an ascent and on the summit of Mt. Everest? A theoretical approach." *High Alt Med Biol* 3(1): 65-8.

At extreme altitude, air has an almost identical composition compared to air at sea level, while its pressure is altitude-dependently lower. When supplementary oxygen is used to achieve an acceptable inspiratory pressure of oxygen ($\text{PI}(\text{O}_2)$) during climbing, the barometric pressure difference to lower altitudes is not compensated for. In this report, we tried theoretically to apply pressure support ventilation (PSV) to partially compensate for low barometric pressures. PSV is widely used for respiratory home care and is applicable via a nasal mask. Since there are light-weight units with long battery lives on the market, we speculated that these units may to some extent replace bottled oxygen. PSV was in theory applied at barometric pressures of 400 torr (Everest Base Camp), 284 torr (South Col), and 253 torr (summit of Mt. Everest). We found that during PSV at a mean airway pressure of 16.5 torr on the summit of Mt. Everest, a fraction of inspired oxygen ($\text{FI}(\text{O}_2)$) of 0.34 sufficed to achieve an alveolar partial pressure ($\text{PA}(\text{O}_2)$) of 67 torr. PSV increases $\text{PI}(\text{O}_2)$ by 3.5 torr, which in theory elevates the maximum oxygen consumption ($\text{V}(\text{O}_{2\text{max}})$) by 218 mL.min^{-1} in an acclimatized climber in this setting. An additional benefit of PSV at extreme altitude may come from the unloading of the respiratory muscles.

Kobayashi, T. (1995). "[High-altitude pulmonary edema in Japan]." *Nihon Kyobu Shikkan Gakkai Zasshi* 33 Suppl: 1-6.

To understand the pathophysiology of high-altitude pulmonary edema (HAPE), we examined the pathway of adaptation to high altitude in lifelong of Tibet. The Tibetan natives had higher exercise performance, but lower maximal oxygen uptake and lower blood lactate concentrations than did acclimatized Han newcomers. Clinical and basic studies done to determine the pathophysiologic characteristics of 47 patients with HAPE and of subjects susceptible to HAPE. The altitude of onset was 2,680 m to 3,190 m above sea level. Results of hemodynamic studies and the presence of protein-rich edema fluid indicated that HAPE is noncardiogenic and is a type of increased permeability edema. The levels of IL-1 beta, IL-6, IL-8, and TNF-alpha in bronchoalveolar lavage fluid from subjects with HAPE were high on admission. The subjects susceptible to HAPE had much greater increases in an index of pulmonary vascular resistance than did the controls, which resulted in much higher levels of pulmonary arterial pressure during both acute hypoxia and hypobaria. The subjects

susceptible to HAPE also has blunted hypoxic ventilatory drives. We studied whether human leukocyte antigen DR-6 functions as a genetic predisposition to HAPE. The frequency of DR-6 was increased in the subjects susceptible to HAPE, which suggests that they have a constitutional abnormality in the pulmonary circulatory, and ventilatory responses to hypoxia and hypobaria, and that genetic factors may be involved in the development of HAPE.

Kolsteren, P. and P. van der Stuyft (1994). "[Diagnosis of anemia at high altitude: problems encountered in Tibet]." *Ann Soc Belg Med Trop* 74(4): 317-22.

To test the hypothesis that Tibetans do not increase their haemoglobin concentration with increasing altitude, haemoglobin concentrations of children aged 6 to 72 months were analyzed. The mean haemoglobin concentrations in the different age groups are significantly lower than the mean concentrations expected at this altitude. Histograms and tests for normality show that the haemoglobin distributions are Gaussian. The probability plots confirm the coefficients of skewness, which indicate a superimposed subpopulation towards the lower range of haemoglobin values. A mixed distribution analysis identifies that the curvilinear deviation found in the probability plot encompasses 10 to 12% of the studied population. Together with the normality of the haemoglobin distributions, we are led to suppose that this is the anaemic population. These figures are considerably lower than those found using recommended cut-off values for this altitude; 40 and 46%. Two possible explanations are put forward: 1) the whole population is submitted to the same factor and hence the whole population should be considered anaemic, 2) Tibetans react differently to altitude than other mountain people and have adapted themselves without increase in haemoglobin.

Leid, J. and J. M. Campagne (2001). "Colour vision at very high altitude." *Color Res Appl* 26 Suppl 1: S281-3.

The goal of our study was to evaluate colour vision during high-altitude mountain climbing without supplemental oxygen. Two Himalayan expeditions were invited to test their colour perception at both the highest possible altitude and on the largest possible number of subjects. The panel desaturated D15 was used, because only a simple test could be transported to those altitudes. There were 2 evaluations (i.e., 4 eyes) at 7,000 m during the first expedition in 1997, and 3 evaluations (i.e., 6 eyes) at 6,500 m during the second expedition in 1998. The results were in perfect agreement and can be considered practically normal for all 5 mountain climbers.

Lhamo, T. (1997). "A one-woman crusade. Interview by David Gough." *Nurs Times* 93(42): 40-1.

Li, Q., R. Sun, et al. (2001). "Cold adaptive thermogenesis in small mammals from different geographical zones of China." *Comp Biochem Physiol A Mol Integr Physiol* 129(4): 949-61.

The mechanisms of thermogenesis and thermoregulation were studied in the tree shrew (*Tupaia belangeri*) and greater vole (*Eothenomys miletus*) of the subtropical region, and Brandt's vole (*Microtus brandti*), Mongolian gerbil (*Meriones unguiculatus*), Daurian ground squirrel (*Spermophilus dauricus*) and plateau pika (*Ochotona curzoniae*) of the northern temperate zone. Resting metabolic rate (RMR) and non-shivering thermogenesis (NST) increased significantly in *T. belangeri*, *E. miletus*, *M. brandti* and *M. unguiculatus* after cold acclimation (4 degrees C) for 4 weeks. In *T. belangeri*, the increase in RMR and thermogenesis at liver cellular level were responsible for enhancing the capacity of enduring cold stress, and homeothermia was simultaneously extended. Stable body temperature in *M. brandti*,

E. miletus, *M. unguiculatus* and *O. curzoniae* was maintained mainly through increase in NST, brown adipose tissue (BAT) mass and its mitochondrial protein content, and the upregulation of uncoupling protein (UCP1) mRNA, as well as enhancement of the activity of cytochrome C oxidase, alpha-glycerophosphate oxidase and T(4) 5'-deiodinase in BAT mitochondria. The RMR in *O. curzoniae* and euthermic *S. dauricus* was not changed, while NST significantly increased during cold exposure; the former maintained their stable body temperature and mass, while body temperature in the latter declined by 4.8 degrees C. The serum T(3) concentration or ratio of T(3)/T(4) in all the species was enhanced after cold acclimation. Results indicated that: (1) the adaptive mechanisms of *T. belangeri* residing in the subtropical region to cold are primarily by increasing RMR and secondly by increasing NST, and the mechanisms of thermogenesis are similar to those in tropical mammals; (2) in small mammals residing in northern regions, the adaptation to cold is chiefly to increase NST; (3) the mechanism of cold-induced thermogenesis in *E. miletus* residing in subtropical and high mountain regions is similar to that in the north; (4) a low RMR in warm environments and peak RMR and NST in cold environments enabled *M. unguiculatus* to tolerate a semi-desert climate.