RE-ENTRY HIGH ALTITUDE PULMONARY EDEMA IN TIBETANS

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High altitude pulmonary edema (HAPE) is known to occur in both sea-level visitors to high altitude (type 1, or entry HAPE) and high altitude residents who return to their native area after a short period of stay at low level (type 2, or re-entry HAPE). The second variety is commonly seen in Peru and Bolivia acclimatized altitude natives of South American (1,2). Also, it is not uncommon even among Leadville residents at 3,100m (3) and there have been occasional reports of HAPE and/or HACE occurring among Sherpas and others, usually at extreme altitude (4,5,6). We know of no previous reported case of HAPE in Tibetan natives. Between 1984 and 1995 we observed a total of 242 cases of HAPE in the Qinghai-Tibetan plateau, among them eight (7 men, 1 woman) were Tibetan native highlanders. Their ages varying form 21 to 37 years. The altitude of onset was 4,280 - 5,520m above sea-level. The diagnosis was based on clinical symptoms, physical signs and radiographic criteria. Seven were pure HAPE, the other one was a mixed form of HAPE with HACE. In all, five were classified as re-entry HAPE. The length of stay at a lower elevation before re-entry to high altitude was 6-21 days. Time-lag between re-ascent and onset of symptoms was eighteen to thirty-two hours. Although the HAPE developed by these Tibetan natives was rather severe, all patients survived. All the patients completed two to four years of follow-up and resumed normal activity in their altitude environment. HAPE will not re-occur as long as they remain at altitude.

These observations of HAPE amongst Tibetans pose many questions, among them three of practical importance:
First, what are the risk factors? Some Tibetans firmly believe that they are adapted, so they rapidly re-ascend to high altitude (for 2-3 days) after a sojourn at a lower altitude, and they will be active after re-ascent, whereas the Chinese Han tourists may be more cautious and ascend slowly (for 3-5 days). All five patients of type 2 (re-entry) HAPE developed it after strenuous exertion following a riding, climbing, or trekking with a heavy load. The other three patients never left Tibet but as a porters ascended by foot to a place much higher than where they usually lived and then fell ill, it was the first time they had been at such an altitude (5480m - 5520m). Therefore, rapid re-entry, acute exposure to extreme altitude, as well as strenuous exertion may be considered risk factors for HAPE in Tibetan natives.

Second, why is there a difference in incidence of re-entry HAPE between the Andeans and Tibetans? The incidence of re-entry HAPE in adults form La Oroya (3750m) in central Peru was as high as 2.6% by Hultgreen and Marticorena (1978)(7). This incidence is much higher than our recently reported (1996) figures of 0.17% to 0.24% of re-entry HAPE in Tibetan natives (8). It has long been known that high altitude natives are more prone to developing HAPE on returning home after a stay at low altitude. However, it seems that the Tibetan native highlanders are an exception. In the first place , this may be mainly related to their very small degree of hypoxic pulmonary vasoconstriction (9). We know that Andean natives have more

muscular pulmonary arteries, the muscle extending to the terminal arterioles (10) and with a higher pulmonary arterial pressure, they seem also to have more reactive pulmonary vascular beds. Previous studies suggest that acute pulmonary hypertension is an important etiologic factor in HAPE (11). This could explain why the re-entry illness is more likely to affect the Andean natives. In contrast, we found the muscular pulmonary arteries of the Tibetans to have a thin-media and the pulmonary arterioles to be devoid of muscles. This may be why the Tibetans are protected against re-entry disease, especially pulmonary edema. Another factor that may be of importance in the pathogenesis of HAPE in Andean natives is erythrocytosis. Prolonged exposure to high altitude results in an increase in blood volume. On descent to sea-level there is a rapid decrease in red cell mass, and this is accompanied by a compensatory rise in plasma volume (12). Thus, if such a person returns to high altitude his increased plasma volume may render him unusually susceptible to pulmonary edema. This may be a contributory factor in explaining why many Andean natives with lung edema at high altitude develop the condition after spending some time at sea-level. In contrast to this, the Tibetans adapt to high altitude without the elevated hemoglobin level and hematocrit values characteristic of Andeans. Tibetans have Hb concentration and hematocrit values within 2 standard deviations of the sea-level values.

Finally, why do Tibetans suffer from re-entry HAPE? Tibetans, as an altitude indigenous population are well adapted. However, variability in sensitivity to HAPE among individuals is found. In one case in our series of patients, a 37-year-old male herdsman, who descended to and spent 12 days at sea level before returning to his altitude home (4280m), the onset of HAPE occurred eighteen hours after reascent. After he had descended to a low altitude (2260 m) and recovered, we measured the pulmonary arterial pressure at a simulated altitude of 4300m, during acute hypobaric hypoxia with strenuous exercise, the mean pulmonary arterial pressure was markedly elevated form 28 to 38 mmHg at rest, rising with exercise to 46 mmHg, with lowered PaO2: from 62 to 48 mmHg at rest and 42 mmHg during exercise. This supports the concept that persons who develop re-entry HAPE have a particular tendency to develop pulmonary hypertension in response to hypoxia. The results suggest that previous acclimatization to high altitude does not always protect a man from pulmonary edema.

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