The Lung at High Altitudes

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In Spain, hundreds of thousands of people travel regularly to the mountains to enjoy sporting activities, such as mountaineering, rock climbing, hiking, and a variety of snow sports. With the advent of globalization in recent years we have also seen an increase in the number of people traveling for work or recreational purposes to areas situated above 2500 meters, where over 140 million people have their permanent home.[1] These visitors very often travel by air, and because most of them do not follow recommended acclimatization procedures they may experience symptoms caused by exposure to altitudes higher than those to which they are accustomed.

Atmospheric pressure decreases with altitude, causing the partial pressure of oxygen in the atmosphere to fall. This lower partial pressure is maintained throughout all stages of the oxygen cascade down to the mitochondria. Populations that have lived for centuries at high altitude (such as the Quechuas and the Sherpas) have adapted by way of a process of natural selection that has involved genetic change.[2] In people who normally reside at or near sea level, however, a series of complex physiological responses must be triggered in a process known as acclimatization. The first of these adjustments is an increase in the frequency and depth of breathing. This is followed by other responses including an increase in heart rate, changes in the oxygen-hemoglobin dissociation curve, an increase in erythropoiesis, and redistribution of arterial flow, all of which serve to increase the delivery of oxygen to the body's tissues.[3] When these compensatory mechanisms are insufficient, acute mountain sickness (AMS) develops. AMS initially presents as a "benign" syndrome characterized by the appearance of a variety of symptoms that may include nausea, vomiting, fatigue, anorexia, headache, vertigo, difficulty sleeping, or dyspnea. If appropriate measures are not taken and the AMS remains untreated, the illness may progress to the more life threatening or "severe" syndromes involving pulmonary and/or cerebral edema.[4-6] Pulmonary edema caused by altitude may be the result of an increase in capillary flow and permeability brought about by nonuniform vasoconstriction of the pulmonary vasculature in response to hypoxia.[6,7]

During recent decades, the scientific community has been interested in investigating the changes in respiratory parameters caused by exposure to high altitude. There have been 2 reasons for this interest: firstly, to identify the changes produced by low barometric pressure and study their causes and mechanisms; and secondly, to find an easy-to-measure parameter with reproducible results that would facilitate the diagnosis of patients with AMS and make it possible to monitor their response to treatment. The primary focus of the few studies published has been to analyze alterations in spirometric parameters and the way these changes evolve on acclimatization. Some of these studies were carried out several decades ago and have important methodological limitations (in statistical treatment, in the calibration of the measuring apparatus used, and/or in the number of individuals studied).[8]

Below 2500 meters, lung function is not significantly altered in most healthy subjects even when arterial oxygen saturation (SaO_2) decreases as a result of a drop in barometric pressure.[9] Over 2500 meters, however, the incidence of AMS symptoms increases as the climbers gain elevation, and above 5000 or 6000 meters some authors have reported a restrictive pulmonary defect in the spirometry of a variable percentage of subjects, a finding that has been associated with the development of interstitial and/or alveolar edema.[8,10-13] In this issue of ARCHIVOS DE BRONCONEUMOLOGÍA, Compte et al[10] publish the results of their analysis of the changes that occurred in the spirometric parameters of 8 mountaineers who climbed to the summit of Mount Aneto (3404 meters) via the standard route. The authors observed a decrease in forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1), but no variation in the ratio of FEV_1 to FVC. Although, for obvious reasons, they were unable to confirm the presence of edema using radiologic techniques, the authors suggest that the changes observed in spirometry may have been related to the development of subclinical

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pulmonary edema. On an earlier expedition, the same authors observed similar changes at 5200 meters.[11] In both studies, the spirometry results improved on acclimatization and returned to normal on descent.

While other researchers[12-15] have reported findings that partially contradict their results, Compte et al point out in their discussion that these discrepancies may be the result of differences in study design. In some studies, subjects at rest were exposed to low barometric pressure in a hypobaric chamber[12]; in other cases there were variations in the altitude at which measurements were taken, in the total altitude difference of the climb, or in the duration of acclimatization.[13] Nor were the populations studied homogeneous with respect to the altitude of the participants' usual residence, the experience of the mountaineers,[14] and the percentage of participants who had previously experienced AMS.[13]

Recently, Cremona et al[15] carried out a prospective "real life" study in an attempt to answer these questions. They set up laboratories at 1200 and at 4559 meters in the Alps and, without preselection, consecutively recruited 262 participants, who were asked to complete a questionnaire at both 1200 and 4559 meters. At both elevations, all participants underwent a detailed physical examination in addition to spirometry, measurement of closing volume, and a chest radiograph. In line with other studies, severe pulmonary edema was the exception,[4-6] with only 1 climber requiring urgent treatment and evacuation. However 15% of the climbers had chest rales and/or radiographic signs of new pulmonary edema despite the fact that they had no significant symptoms to suggest it. The climbers who developed subclinical pulmonary edema showed decreases in FVC and increases in closing volumes, but no significant alterations in FEV_1 or midexpiratory flows. Conversely, in the group of climbers who did not develop pulmonary edema an increase was observed in FEV_1 and particularly in midexpiratory flows, but there were no changes in FVC. These results are similar to the findings reported by other authors[12-14] and may be related to the effect of lower air density on airway flow. The presence of edema would, however, counteract this beneficial effect and could, if the edema were sufficiently severe, even cause a decrease in respiratory flows and volumes.

There may be a broad spectrum of responses to exposure to hypobaric hypoxia, in which case the development of edema would vary depending on a series of factors, such as those listed above, but would also depend on individual differences. For example, certain polymorphisms in the angiotensin-converting enzyme gene could have a protective effect,[16] and other genes may mediate an exaggerated hypoxic pulmonary vasoconstrictor response accompanied by pulmonary hypertension.[17] While the precise mechanism of this vasoconstrictor response is still poorly understood, an endothelial dysfunction that leads to a reduction in the synthesis of vasodilators such as nitric oxide[18] and/or an increase in the formation of vasoconstrictors such as endothelin-1 has been observed in susceptible individuals.[19] The administration of sildenafil has a beneficial effect on pulmonary hypertension and exercise capacity.[20,21] This finding tends to support the hypothesis that mechanisms mediated by nitric oxide are involved in the development of edema.

In the article published in this issue of ARCHIVOS DE BRONCONEUMOLOGÍA, Compte et al[10] report that SaO_2 results correlate closely with the symptoms of AMS and with acclimatization. In an earlier study, those authors saw correlations between declines in SaO_2 and elevation up to 4230 meters in a group of mountain climbers.[22] Some researchers[23] have argued against the use of pulse oximetry as a technique for diagnosing AMS. They cite the following drawbacks in support of this position: the fact that individual values overlap between the groups with and without symptoms; the marked interindividual variability in SaO_2 values; the lack of accuracy of SaO_2 values under 80%; and the possibility of erroneous measurements caused by peripheral vasoconstriction brought about by cold or false high values secondary to hyperventilation triggered by fear or anxiety. However, further studies including individuals who present the signs and symptoms of AMS are needed to assess whether SaO_2 values could be used to support decisions concerning the treatment and management of this syndrome in an environment that can be hostile. A small portable pulse oximeter would not only become an indispensable tool for doctors working in hospitals located at high altitudes, but would also be an essential piece of equipment in the first aid kit carried by mountaineers and trekkers on high altitude expeditions because the diagnosis of AMS in the mountains has until now depended entirely on the appearance of symptoms.[3] It would also be interesting to ascertain whether monitoring SaO_2 and other easily measured spirometric parameters[23] could facilitate the management of AMS.

Mountain climbing is a sport that has proved to be a rich source of knowledge of interest to scientists in many different fields going far beyond the boundaries of the sport itself. Some excellent respiratory specialists and physiologists have been distinguished mountaineers[1,2] and have led numerous important scientific and sporting expeditions. The scientific information obtained on such expeditions has given us a better understanding of the limits of human physiology. The exposure of humans to high altitude is probably the best experimental model of subacute and chronic respiratory failure we have today. In several countries research groups have been established to work permanently in high altitude laboratories, and in others, such as Great Britain, scientific expeditions are preparing to set out in the near future. Studies on respiratory physiology will play a leading role in these expeditions, which will have an exclusively scientific purpose.[24] While Spain is a country with a highly accomplished mountaineering community, our research in the area of high altitude medicine is surprisingly meager in view of the country's

mountainous topography and sporting, scientific, and economic strength. We must, therefore, encourage and applaud any research undertaken by Spanish scientists in this field and commend the editors of the scientific journals who support their work by publishing the results.

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