Lessons from High Altitude Pulmonary Edema

Fifty years ago, Barcroft pointed out that much could be learned about normal transport of oxygen by studying sojourners and residents at high altitude. More recently, Severinghaus has commented on the relevance of such studies to patients with a lack of oxygen at sea level; for instance, acute mountain sickness is common above 1,900 meters (6,324 feet), and its severe headache, nausea, and mental confusion resemble the symptoms of carbon monoxide poisoning, which also reduces arterial oxygen saturation. High altitude pulmonary edema often appears above 2,700 meters (8,858 feet); and its dyspnea, blood-stained sputum, and patchy pulmonary infiltrates are much like those seen in the acute (adult) respiratory distress syndrome or "shock lung" and in the pulmonary edema following heroin overdosage or near drowning. Brain or cerebral edema at altitude is similar to that seen in carbon monoxide poisoning or during surgery on the brain if the patient becomes hypoxic. The retinopathy found in half of all people going above 5,300 meters (17,727 feet) resembles that observed in many patients with chronic pulmonary disease. Other analogies between the healthy mountaineer and the sick or injured person with a lack of oxygen are being recognized.

Ravenhill in 1913 was the first to clearly define the different forms of altitude sickness, which he saw at 4,200 meters (13,775 feet) in the Andes, calling the forms "normal puna" (which we call acute mountain sickness), "cardiac puna" (our high altitude edema), and "nervous puna" (which he applied to cerebral edema). Today we believe that these form a continuous spectrum, rather than separate entities, but there remains some uncertainty as to their basic pathophysiology. Most favored today is the theory that lack of oxygen disrupts the adenosine triphosphate-dependent sodium pump (which maintains normal distribution of water and electrolytes between intracellular and extracellular spaces) and that, as a result, edema accumulates here and there in the body, depending on vulnerabilities not clearly understood.

High altitude pulmonary edema is the most common of the serious manifestations of altitude sickness and has been most studied in recent years. Like the other forms (but more frequently), high altitude pulmonary edema strikes "the young, the fit, the enthusiastic, the audacious and the hardworking" or as Rennie put it, because these are the most numerous visitors to high altitude, providing a series of natural experiments from which much can be learned. Their illnesses and occasional deaths pose many questions, among them two of practical importance: (1) How likely is the person who has one bout of high altitude pulmonary edema to have another? (2) How accurate is the impression that residents at altitudes are more susceptible to high altitude pulmonary edema when they reascend after a stay at low altitude?

Elsewhere in this issue (see page 372), Hultgren and Marticorena present evidence that high altitude pulmonary edema is several times as frequent among reentrants as in new arrivals. Several months ago, Scoggin et al published similar data from Leadville, Col (altitude, 3,300 meters (10,827 feet)). Both studies conflict with that of Singh et al, who reported that among 332 soldiers taken rapidly to 3,300 meters or higher, the incidence of high altitude pulmonary edema was 16 percent in reentrants, compared to 13 percent among new arrivals. Both of these figures are very much higher than expected, presumably due to the rigor of combat, in which altitude is said to have caused more casualties than the action of the enemy. If the studies by Hultgren and Marticorena and by Scoggin et al are correct, then residents of altitudes who spend a short time at low altitude should take particular care to return home slowly, to avoid exertion, and to get appropriate treatment at first evidence of distress.

Both studies lack data showing how many returnees did not develop high altitude pulmonary edema on reentry, and, therefore, the incidence cannot be accurately determined for comparison with the crude estimates of the incidence of high-altitude pulmonary edema among new arrivals. Ravenhill recognized the problem when he said, "acclimatization tends to protect them [residents] on their return from lower levels," but he added that some of his 35 patients developed altitude sickness after each return, some never did, and others were affected.
only occasionally. The puzzle has many pieces, such as the general health of the individuals, the intake of salt and water, underlying pathologic conditions (three persons developing severe high altitude pulmonary edema edema at only 2,900 meters [9,514 feet] were found to have previously unsuspected congenital absence of one pulmonary artery), or individual idiosyncrasies. Hultgren et al8 found by studying six persons who previously had several bouts of high altitude pulmonary edema that their pulmonary arterial pressures rose to much higher levels than the normally elevated pressures usually found at altitude, even though none of the six subjects showed evidence of high altitude pulmonary edema at the tested altitude of 4,600 meters (15,092 feet).

Hultgren et al and Scoggins et al9 have made impressive cases. What might be some of the clinical implications? Obviously, one must warn the victim of high-altitude pulmonary edema about the need for extra precautions when returning to altitude after a brief stay lower down, and one should probably caution persons who have had more than one or two bouts to be particularly careful on subsequent visits to altitude. Are there some lessons for persons at sea level, too?

Thousands of persons are severely hypoxic at sea level, due to pulmonary insufficiency from one cause or another; in effect, they live at altitude, often higher than 3,500 to 4,500 meters (11,483 to 14,784 feet) in terms of oxygen in the blood. Occasionally, these persons must be given therapy with supplemental oxygen, bringing them, as it were, down to low altitude. Do they become more vulnerable to pulmonary or cerebral edema when treatment is stopped? Acute pulmonary edema after near drowning or near fatal heroin overdosage or during and after prolonged shock is not uncommon and may be due to acute hypoxia like that during rapid ascent; but in some instances, pulmonary edema appears when the crisis seems over, after therapy has been halted. Are these experiences equivalent to edema developing on reaescion after a period in an environment with normal oxygen? Recently, it has been shown that arterial oxygen saturation falls sharply during sleep, probably due to disturbed breathing patterns. Well known is the exacerbation of symptoms during the night and in the early morning among patients with chronic pulmonary conditions. Is the sudden infant death syndrome, which is remarkably more common during sleep, in any way similar to high altitude pulmonary edema after reaescion? If so, could some of the preventive measures used by climbers benefit the sick? Therapy with acetazolamide (Diamox), nikethamide (Coramine), or medroxyprogesterone 17-acetate (Provera) has been proven of value to mountaineers; will these medications help the hypoxic ill patient or infants vulnerable to sudden infant death syndrome as well? Would the ability of phenytoin sodium (Dilantin) to stabilize membranes decrease the migration of salt and water and thus diminish high altitude pulmonary edema, cerebral edema, and acute mountain sickness? Should such medicines be recommended to those returning home after a stay at low altitude? The study by Hultgren and Marticorena and many other studies at altitude should provoke new thoughts about persons with a lack of oxygen at sea level, as well as those going to high altitude.

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REFERENCES
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Tachycardia Induced by Atrial Pacing

Tachycardia induced by atrial pacing is widely employed in the evaluation of patients with pain in the chest. Tachycardia is a simple method of increasing left ventricular work and producing myocardial ischemia. Evidence of myocardial ischemia can be monitored easily in the catheterization laboratory by assessing electrocardiographic, hemodynamic, and myocardial metabolic changes. Furthermore, the ischemic state induced by atrial pacing disappears rapidly when sinus rhythm is restored, thus providing a safety factor unavailable in other forms of stress (eg, exercise or infusion of isoproterenol). Atrial pacing does not replace exercise stress tests for the evaluation of patients with ischemic heart disease. Instead, atrial pacing is a supplementary technique that makes it possible to examine left ventricular hemodynamics, coronary blood flow, and myocardial metabolic function be-