Into Thin Air

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Mountain climbing is more than a risky but increasing popular recreation. Past investigations of the effects of high-altitude hypoxia in climbers have provided data used to guide O₂ therapy in patients and treat pulmonary edema [1].

Research on adaptations to hypoxia has had a resurgence with studies using recently developed cellular techniques as well as the more traditional methods of measuring ventilation; and these new studies promise to ultimately lead to new ways of treating patients. A study of the more traditional sort appears in this issue of *Respiration* [2].

Serebrovskaya and co-workers [2] compare changes in hypoxic ventilatory sensitivity in elderly and younger individuals with exposure to altitude. They try to relate these differences to changes in blood levels of dopamine and find some significant correlations which might explain age-dependent differences. Cause and effect are difficult to demonstrate in this sort of study, so that the data though interesting allow no firm conclusions to be reached. Studies in animals and in the isolated carotid body have shown that while dopamine is involved in modulating the carotid body signal, its effects are excitatory in some species, but inhibitory in others [3]. The neurotransmitter(s) responsible for the excitatory effects of low oxygen in humans is still unknown and candidate transmitters include acetylcholine and the neurokinins, as well as dopamine [4].

Using new methods, current research has explored the cellular pathways in vitro which mediate effects of hypoxia and has identified actions of hypoxia on the potassium and calcium channels of type I cells which lead to depolarization and neurotransmitter secretions [5, 6].

It has also been shown in vitro that hypoxia can act directly on other types of cells such as those in blood vessels, the heart, the liver, and the kidneys by affecting specific genes (early immediate response genes) and by altering the levels of hypoxia-inducible factor-1 which accelerates the formation of specific proteins [7–9]. The early immediate genes are involved in accelerating tyrosine hydroxylase production (the rate-limiting enzyme in dopamine formation) while HIF-1 (a protein present in small amounts in cells), in addition to raising intracellular tyrosine hydroxylase by binding to the enhancing regions of genes, also orchestrates the production of a number of different substances (such as erythropoietin) helpful in survival under hypoxic conditions.

These intracellular changes have been demonstrated under in vitro conditions in which the ambient O₂ levels are decreased as they are at altitude. Hypoxia though is far more common as arterial hypoxemia arising from lung disease or sleep apnea. If it can be confirmed that hypoxemia has similar effects in humans, as it does in cell culture, it may be possible to develop interventions in addition to breathing oxygen which can modulate specific adaptive reactions and which can be targeted to the benefit of the patient.

References

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