reinfarction, there was a statistically significant benefit demonstrated for enoxaparin vs unfractionated heparin in the full-dose tenecteplase group (4.4% vs 15.9%, log-rank $P=.003$) that was attenuated in the combination therapy group (5.5% vs 6.5%, $P=.67$).[3] We believe that the superior efficacy of enoxaparin vs unfractionated heparin, as well as the unequal and nonrandom use of these agents in these 3 trials, confound the results of the meta-analysis.

Individual trial data may be more illuminating. Compared with conventional treatment of STEMI with full-dose fibrinolytic drugs and unfractionated heparin, the use of half-dose fibrinolytic drugs, adjunct abciximab, and unfractionated heparin confers efficacy benefit, while the use of full-dose fibrinolytic drugs and enoxaparin confers both efficacy and safety benefits.[2] However, when adjunctive abciximab is used in combination with enoxaparin, the benefits are not additive.[3] We believe that the choice of using adjunctive abciximab or enoxaparin in individual patients with different levels of risk remains undetermined but will ultimately be superseded by cost considerations.

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In Reply: We agree with Dr Tan and colleagues that the use of low-molecular-weight heparin has the potential to be a confounding factor in our meta-analysis, particularly in the results of trials with thrombolysis, whereas unfractionated heparin was used in all primary angioplasty trials. However, we believe that actual confounding is unlikely. The support for this hypothesis comes from a post hoc observation of a small trial (ENTIRE-TIMI 23),[1] whereas the largest trial included in the meta-analysis (GUSTO V)[2] showed that in patients treated with unfractionated heparin, combination therapy does not give any additional benefit in terms of mortality. Furthermore, no data on the comparison between thrombolysis plus abciximab in patients receiving unfractionated heparin vs low-molecular-weight heparin have been reported in the ASSENT-3 trial.[3] Finally, in our study we analyzed death and reinfarction as separate end points, whereas the data cited from the ENTIRE-TIMI 23 trial[1] are based on a combined end point of death, reinfarction, or both.

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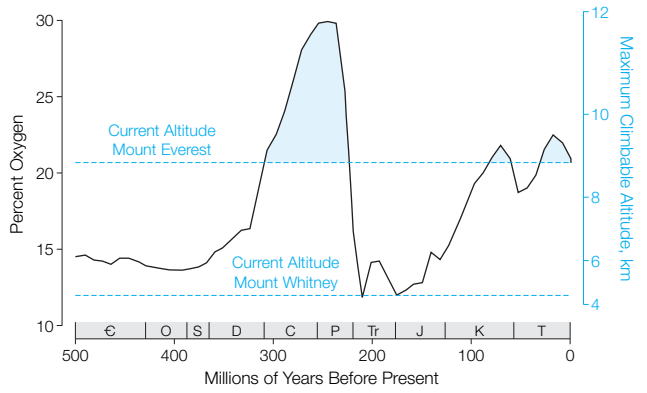
RESEARCH LETTER

Climbing a Triassic *Mount Everest*: Into Thinner Air

To the Editor: At a height of 8850 m, Mount Everest has long been a magnet to Himalayan mountaineers, and its summit has been reached 2251 times through 2004.[1] Because 130 of those ascents were made without supplemental oxygen,[1] contemporary humans are undoubtedly capable of climbing higher than 8850 m without supplemental oxygen, if a higher summit were available. The upper limit for mountaineers has probably varied over time because atmospheric oxygen concentrations (currently 20.9%) have changed drastically over the past 570 million years.[2] We simulated how these oxygen shifts would have affected the maximum altitude reachable by hypothetical "paleo-mountaineers."

Methods. To estimate past maximum potential altitudes, we first determined the maximum altitude reachable in today's atmosphere. West[3] calculated that Mount Everest's summit should be close to the limit of human climbing without supplementary oxygen. Consistent with this, we used 9.0 km as a conservative limit. This is feasible because it approximates the "physiological" altitude reached by Sherpa Ang Rita when he summited Mount Everest without using supplemental oxygen on December 22, 1987. The estimated summit partial pressure of inspired oxygen (P_{IO_2}) on that winter day was physiologically equivalent to 9.0 km during the customary spring climbing season when P_{IO_2} is

Figure. Change in Percent Oxygen and in the Maximum Climbable Altitude Reachable by "Paleo-Mountaineers" Over Geological Time



Geological periods: Є, Cambrian; O, Ordovician; S, Silurian; D, Devonian; C, Carboniferous; P, Permian; Tr, Triassic; J, Jurassic; K, Cretaceous; T, Tertiary. Blue shading indicates times with sufficient oxygen for ascents of a peak the height of Mount Everest to be summited without using supplemental oxygen. The intervals on the right vertical axis (maximum climbable altitude) are not equal because the relationship between percent oxygen and maximum climbable altitude is nonlinear.

higher.[4] Although Bailey[5] recently proposed a much higher limit (9972.7 m), his estimate was incorrectly based on a linear (rather than curvilinear) regression model and is unrealistic given slow climbing rates at extreme altitude.

We used a model atmosphere equation for barometric pressure vs altitude[4] to compute present-day P_{IO_2} at 9.0 km, and then used this amount as the minimum level tolerable by both present-day and hypothetical paleo-mountaineers. We next expanded an equation[4] for P_{IO_2} as a function of percent oxygen and of the summed partial pressures of oxygen and of nitrogen (including minor gasses, all assumed constant over time[2]). We then corrected the P_{IO_2} for percent oxygen, and solved for altitude.[6] This estimated the maximum altitude reachable under a given percent oxygen. We assumed that maximum altitude is determined only by P_{IO_2} and ignored minor effects of concurrent climate change[6] and of uncertainty in percent oxygen.[2]

Results. During the mid-Permian era, oxygen was relatively abundant[2] and P_{IO_2} is thought to have reached approximately 30 percent (FIGURE). By the early Triassic era, however, P_{IO_2} fell to approximately 12%.[2] Shifts in oxygen concentration would have dramatically altered the maximum climbable altitude over time (Figure). During the Permian high oxygen concentration, hypothetical paleo-mountaineers would have been aerobically capable of reaching nearly 12 km, about one third above the current summit of Mount Everest. During the Triassic low oxygen concentration, climbers would have been stopped at 4.5 km, below the summit of Mount Whitney (4.4 km). A prehistoric Ang Rita would have been incapable of reaching a Triassic base camp on Mount Everest (5.3 km).

Comment. On a geological scale, neither Mount Everest nor humans existed until recently. Nevertheless, our findings add a novel, deep-time perspective on high-altitude physiology and medicine. Our analysis suggests that peaks as high as Mount Everest would have been physiologically reachable by humans during less than one third of the past 570 million years. Thus, it is only through a fortunate accident of geology and biology that humans evolved and have always lived during a time in which oxygen levels have been sufficiently high to allow (a few of) us to reach the highest summit on Earth.

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CORRECTION

Incorrect Labels in FIGURE: In the 3-page timeline foldout entitled "Albert Lasker Medical Research Awards, 60 Years of Basic Discoveries and Clinical Advances" published in the September 21, 2005, issue of JAMA (2005;294:1426 A-F), the labels indicating RNA bases and amino acids were incorrect. The labels for the RNA bases should have read U instead of T, and labels for amino acids should have read (from 5′ to 3′) Ala, Val, Phe.

The detail is reproduced below at full size and can be cut out and affixed to the original poster.