intravenous cefuroxime plasma creatinine concentration rose to 383 $\mu\text{mol/l}$ (4.3 mg/100 ml) (calculated creatinine clearance 14.5 ml/min) after three days. Ibuprofen was stopped, and within 10 days plasma creatinine concentration was 135 $\mu\text{mol/l}$ (1.5 mg/100 ml).

Comment

Acute renal impairment in acute pyelonephritis is rare; patients are normally predisposed to it if they have underlying renal disease such as chronic pyelonephritis, papillary necrosis, or obstructive uropathy.¹ Three of our patients had evidence of underlying renal disease, but the fact that all four patients were taking non-steroidal anti-inflammatory drugs raises the possibility that in patients with either underlying renal impairment or urinary infections these drugs may predispose to both acute pyelonephritis and acute renal impairment. Other renal side effects are well documented.² The mechanism for what we have described might be an abnormality of immune function or of autoregulation of renal blood flow secondary to impaired synthesis of prostaglandin.³

We suggest that non-steroidal anti-inflammatory drugs should be prescribed with caution in patients with renal impairment, chronic pyelonephritis, or recurrent urinary infection.

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Increased capillary fragility at high altitude

Since the observation by Frayser *et al* of retinal haemorrhages in people at high altitude¹ there has been debate about their cause as well as the effect of altitude induced hypoxia on other body tissues. Most theories propose that vessel wall weakness and increased intraluminal pressure rather than platelet dysfunction are responsible for high altitude retinal haemorrhage. Other haemorrhagic phenomena reported at high altitude include microscopic haematuria, subungual splinter haemorrhage, buccal mucosal haemorrhage,² and widespread cerebral capillary haemorrhage.³ We used the method of mucosal petechiometry to examine the relation between capillary fragility and increasing altitude.

Subjects, methods, and results

The subjects of this experiment were three healthy white men on a climb of the Indian Himalayan peak Jogin 1, 6465 m (21210 ft). Capillary fragility was measured using the method described by Stirrups *et al*.⁴ This entailed placing a 1 cm plastic bell on the mucous membrane on the inner aspect of the lower lip. A negative pressure of 200 mm Hg was applied for one minute, sucking the mucosa up into the bell. The petechiae so produced were counted by two observers and the results averaged. We tested two sites on each occasion and summed the results. With the exception of the sea level controls all observations were made within 24 hours of arrival at a specified altitude. We also used a positive pressure test—the tourniquet (Hess) test. Funduscopy was performed at base camp, 4750 m (15580 ft), before and after the climb. Least squares regression analysis was used to test the association between altitude and number of petechiae.

The figure plots against altitude the total number of petechiae in the three subjects at each altitude. The equation of the least squares regression line was $y = 2.20 + 2.44x$, and the associated correlation coefficient was 0.54. The slope of this line was statistically significant at $p < 0.02$ in a two tailed test.

Tourniquet test—A maximum of eight petechiae were seen in any one test (up to 10 may be normal) and there was no correlation with altitude. This is consistent with the observation in haematological practice that the tourniquet test is, at best, a poor predictor even of major degrees of capillary fragility.⁵

Funduscopy—At base camp before the climb fundal examination showed dilated and tortuous vessels in all three climbers. On return 11 days later

appearances were unchanged in two subjects. The third (subject 1) had two retinal haemorrhages in his right eye and three in his left. All fundi were normal 10 days later.

Acute mountain sickness—Two subjects experienced only the normal dyspnoea of high altitude. Subject 1 experienced moderate acute mountain sickness on ascent, complaining of dyspnoea on exertion, headache, anorexia, and lethargy.

Change in petechiae count with altitude in subjects 1 (■), 2 (●), and 3 (○). d = Observations made on descent.

Comment

These results show that there is an increase in capillary fragility with altitude. The technique used is important for two reasons. Firstly, it detects increased capillary fragility in subjects in whom spontaneous capillary rupture is not observable. This is evidence that increased capillary fragility is a widespread effect of high altitude on the microvasculature. This phenomenon may contribute to the pathogenesis of acute mountain sickness and its life threatening variants, high altitude pulmonary oedema and high altitude cerebral oedema. Secondly, the method might be used to try to determine which components of the high altitude environment affect capillary fragility. Pressure chamber experiments could examine the relation between hypoxia, hypobarism, drug prophylaxis, and capillary fragility.

Of the three subjects studied, the one with consistently more fragile capillaries (subject 1) was the only one to suffer both retinal haemorrhage and acute mountain sickness. It is interesting to speculate that an intrinsically high capillary fragility may predispose a person to capillary leakage or rupture and thus acute mountain sickness. If this were so, then capillary fragility at sea level may be a predictor of performance at altitude.

Given the small number of subjects in this experiment, however, the results should be interpreted with caution. More data are needed before a complete understanding of the relation between capillary fragility and altitude will be possible. We should expect the important factor of acclimatisation to modify this relation.

We hope that this pilot study will prompt further work in this area. If confirmed in a larger series petechiometry may prove a useful tool in the continuing search for an understanding of the pathogenesis of acute mountain sickness and other hypoxic disease.

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