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Sir—Damian Hoy and co-workers[1] point out the high prevalence of low back pain in rural Tibet, and suggest an interesting cure, consisting of "back-happy" tap-stands. Another intervention could involve changing the inhabitants' attitude towards work-sharing between men and women. In the two photographs presented, the woman carries the water—there being twice as many "happy" men watching.

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1 Hoy D, Toole MJ, Morgan D, Morgan C. Low back pain in rural Tibet. *Lancet* 2003; **361:** 225–26.

Sir—Damian Hoy and colleagues[1] report on the particularly high prevalence of low back pain in rural Tibet. However, low back pain is only one of the many problems affecting health in rural Tibet, and we think that this issue can be placed in a wider perspective.

The nutritional context of rural Tibet probably has a major role in the occurrence of osteoarticular disease in this region. From infancy, inhabitants of rural Tibet are exposed to severe deficiencies of micronutrients such as iodine, selenium, and vitamin D.[2,3] Iodine and vitamin D deficiency can both affect bone health in growing children, and long-term vitamin D deficiency can increase the risk of osteoporotic fracture in adults.

The frequency of low back pain in Hoy and colleagues' study was higher in women than men; some of these women could have osteoporotic fractures. Selenium deficiency has been associated with the occurrence of Kashin-Beck disease—an osteoarthropathy endemic in Tibet, which causes joint deformation and limited joint mobility.[2] Along with these epidemiological data, we have shown experimentally that selenium deficiency is associated with osteopenia.[4] We would therefore be interested to know the prevalence of osteoporosis and vertebral fractures among the individuals with low back pain, particularly the women.

We should not let hidden hunger go undetected as a cause of low back pain in Tibet, since prevention might warrant more causal interventions.

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Mechanical ventilation and multiple organ failure

Sir—In their excellent Review, Liao Pinhu and colleagues (Jan 25, p 332)[1] postulated that mechanical ventilation induces pulmonary production of inflammatory mediators, which exacerbate lung injury. Moreover, they suggested that overspill of these mediators into the systemic circulation of patients could contribute to multiple organ failure. Proinflammatory cytokines—eg, tumour necrosis factor (TNF) α and interleukin 6—and chemokines—eg, macrophage inflammatory protein-2 (MIP-2)—play a crucial part in this process.[2,3] But how do these mediators exert their detrimental effect on distal organs? There is no direct evidence for the theory suggested by Pinhu and co-workers, since in-vivo lung-derived inflammatory mediators cannot be labelled. Furthermore, even if proinflammatory mediators do spill over, whether they induce a peripheral response as well as a response in the lungs remains questionable.

In 12 infants without lung injury, we noted an increase in TNF α and interleukin 6 concentrations in bronchoalveolar fluid after 2 h of mechanical ventilation with a tidal volume of 10 mL/kg and a positive end respiratory pressure of 4 cm H_2O.[4] However, the capacity of their peripheral blood lymphocytes to produce interferon gamma was decreased and, after stimulation with lipopolysaccharide, monocytes released less interleukin 6 and TNF α. Additionally, the activity of natural killer cells was decreased. We confirmed this phenomenon of peripheral immunosuppression in healthy rats and in lipopolysaccharide-treated rats that had been ventilated for 4 h with several ventilatory strategies.

These findings suggest that ventilation induces systemic immunosuppression as well as an acute proinflammatory response in the lungs, and questions the theory that peripheral inflammation in distal organs is caused by proinflammatory mediator overspill from the lung.[5]

Furthermore, the presence of cytokines in tracheal aspirates does not necessarily imply ventilator-associated lung injury. Under certain conditions, mechanical ventilation could simply trigger a complex but well balanced sequence of proinflammatory and anti-inflammatory mediators aimed at achieving appropriate lung healing and restoring homoeostasis. This adaptive inflammatory response does not primarily cause lung injury. If, however, a disturbance in the balance between proinflammation and anti-inflammation takes place, for example due to the presence of a persistent injurious ventilatory strategy or pre-existing lung injury, a deleterious inflammatory response could prevent satisfactory lung healing and lung injury might develop or be exacerbated. The latter process could be treated effectively by local application of anti-inflammatory drugs. Whether or not multiple organ failure is the result of the poor balance in proinflammatory and anti-inflammatory pulmonary cytokine production in these conditions has not been proven. However, strategies aimed at reversing the effects of peripheral immunosuppression need to be developed to prevent multiple organ failure.

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