HIV-1 and scrub-typhus

Sir—George Watt and colleagues[1] provided evidence that acute scrub–typhus infection suppresses HIV-1. They showed that serum samples from typhus-infected patients and mice had an inhibitory effect on HIV-1 in vitro. This finding suggests that some humoral factor induced in scrub-typhus suppresses HIV-1 viral load. Watt and colleagues measured serum concentrations of tumour necrosis factor α (TNFα) in patients with and without scrub-typhus, but the results were inconclusive. How then might scrub-typhus inhibit HIV-1? A strong contender is interferon gamma. Interferon gamma produced in response to scrub–typhus in mice[2] and human beings,[3] suppresses HIV-1.[4] We have shown that concentrations of activated T cells, which can secrete interferon gamma,[4] are greatly increased in the peripheral blood of patients with scrub-typhus.[5] Study of the suppression of HIV-1 by scrub-typhus should include interferon gamma and activation markers on T cells.

*Masayuki Ikeda, Shohji Yoshida

*Department of Clinical Research, National Saigata Hospital, Ohgata-machi, Niigata 949-3193, Japan; and Department of Medicine, Asahi General Hospital, Asahi, Chiba, Japan (e-mail: massie@saigata-nh.go.jp)

1 Watt G, Kantipong P, de Souza M, et al. HIV-1 suppression during acute scrub-typhus infection. *Lancet* 2000; **356:** 475–79.
2 Jerrels TR, Li H, Walker DH. In vivo and in vitro role of gamma interferon in immune clearance of Rickettsia species. *Adv Exp Med Biol* 1988; **239:** 193–200.
3 Ikeda M, Yoshida S, Tsukagoshi H. Interferon-γ in cerebrospinal fluid without pleocytosis in scrub typhus. *J Neurol Sci* 1992; **109:** 61–63.
4 Bailer RT, Holloway A, Sun J, et al. IL-13 and IFN-γ secretion by activated T cells in HIV-1 infection associated with viral suppression and a lack of disease progression. *J Immunol* 1999; **162:** 7534–42.
5 Ikeda M, Takahashi H, Yoshida S. HLA-DR$^+$CD3$^+$ and CD8$^+$ cells are increased but CD4$^+$CD45RA$^+$ cells are reduced in the peripheral blood in human scrub typhus. *Clin Immunol Immunopathol* 1994; **72:** 402–04.

Bone density in cosmonauts

Sir—Some features of Laurence Vico and colleagues' report (May 6, p 1607)[1] on microgravity exposure and volumetric bone density seem obscure.

Initially, 22 astronauts were included in the study but only 11 were followed up statistically without comparison with controls unaffected by microgravity. Human beings, when on earth, lose bone mass and density comparably in the same age-groups and time. Which changes would have been measured in the non-orbiting group? Vico and colleagues do not explain the difference in methods between volumetric and area projected bone density or mass. Such explanation might substantially affect interpretation of the data.

The results are presented almost solely for bone effects. Vico and colleagues missed the chance to view the results in terms of the interactive dependence of the musculoskeletal system, with the use of microgravity as an ideal experimental platform.

Despite use of a method that could evaluate structural and mechanical properties of bones, Vico and colleagues provide no information about the magnitude of the effect of physical activities on bone mass, strength, and architecture. Without the Earth's gravity, the primary function of bones to provide rigid levers for muscles is lessened (or extremely facilitated). In 1892 Julius Wolf suggested that adaption of shape and architecture on Earth is achieved through stresses on bone to make efficient and light weight use of the material. This view implies that the adaptation of bones in later life is dynamically controlled by a feedback mechanism based on physical loading, presumably through minimum effective strains.[2] Disuse, such as during space flight, triggers remodelling and increases loss of bone, mostly next to the marrow. That combination of mechanisms leads to osteopenia and shorter thinner bones.

Sudden decline in necessary muscle strength accompanies a decline in muscle mass.[3] This observation should have given Vico and colleagues reason to investigate the effects of microgravity on muscle strength or mass in relation to bone strength and density. Therefore, they should have used peripheral quantitative computed tomography (pQCT) to provide some accurate non-invasive measures of cross-sectional bone strength and muscle features that might affect bone.[4]

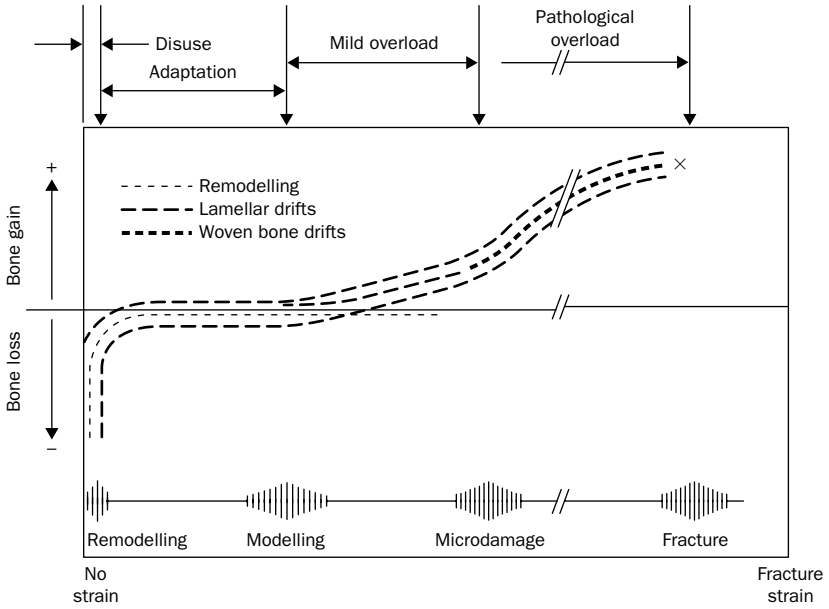
Changes in bone mass can be described by two complementary assumptions. Modelling and remodelling should adapt bones' strength to the greatest strains, which originate from muscle forces (figure).[5] Ineffective training activities during space flight not designed to reach the minimum effective strain level might be the cause of bone loss in the lower limbs. This theory would accommodate Vico and colleagues' observations.

Although changes in bone microstructure due to microgravity might be interesting, such study investigates only material property that nature supplies to achieve maximum strength and architectural competence. Fundamental understanding would be gained from identification of strain patterns on bone.

*Peter Schneider, Christoph Reiners

Clinic for Nuclear Medicine, University of Würzburg, 97080 Würzburg, Germany

1 Vico L, Collet P, Guignandon A, et al. Effects of long-term microgravity exposure on cancellous and cortical weight-bearing bones of cosmonauts. *Lancet* 2000; **355:** 1607.
2 Frost HM. Skeletal structural adaptations to mechanical usage (SATMU: I. Redefining



Effect of modelling and remodelling on bone strength and mass