

# Bone and the Gulf War

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## Osteoblasts—possible victims of the Gulf War?

Compston and her colleagues have a deserved international reputation for their studies of bone turnover and altered bone cell function in skeletal disease. Recently, they have been approached to undertake studies of bone in groups of individuals concerned about the possible harmful effects on their bone of exposure to environmental toxins. The paper published in this journal<sup>1</sup> describes the results of an examination of bone from 17 veterans of the Gulf War and follows relatively shortly after a paper published in 1999 looking at the bone of farm workers exposed to organophosphate insecticides.<sup>2</sup>

A proportion of Gulf War veterans from several countries including the USA, Canada, and the UK complain of a variety of symptoms such as fatigue, lack of sleep, depression, cognitive problems, rashes, bone aches, lassitude, lack of motivation, forgetfulness, mood changes, irritability, and diarrhoea. If these symptoms sound non-specific and ones that perhaps we all experience from time to time, it is hardly surprising that there has been a degree of scepticism about their importance. Epidemiological studies of large populations have not helped to resolve the problem of whether or not "Gulf War syndrome", as the symptom complex has become known, is a "war related illness".

However, in the context of the current paper, it is worth noting that one group who approached the problem in a different way showed that Gulf War veterans suffered proportionately more hospitalisations for certain specific diagnoses, including fractures and bone and soft tissue injuries.<sup>3</sup> This study examined the proportional morbidity ratios of hospitalisation discharge diagnoses (both broad symptom complexes and specific diagnoses) between Gulf War veterans and other veterans of the same era.

The study of Compston *et al* has examined bone mineral density using dual energy x ray absorptiometry, and bone matrix type and distribution and bone cell function using image analysis based bone histomorphometry. Very briefly, they showed that although the bone biopsies showed "considerable heterogeneity" across the 17 Gulf War veterans there was a significant ( $p = 0.027$ ) reduction in the amount of cancellous (trabecular) bone and a decrease in osteoblast activity and therefore bone formation ( $p < 0.0001$ ). Although osteoclast numbers were reduced, the extent of bone surfaces showing evidence of erosion was increased. Because eroded surfaces remain visible until they are filled in by osteoid deposited by osteoblasts, this apparent anomaly can be explained on the basis of failure of osteoblasts to cover over eroded surfaces, rather than an absolute increase in osteoclasts.

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Clearly, people who are debilitated and depressed take less exercise and may indulge in "comforting" habits such as smoking and drinking alcohol to excess. The authors could not find a connection between these activities and bone abnormalities in their group, but accept that in a group of this size the possibility of an effect from life style changes cannot be excluded.

The authors try to identify a possible cause for the changes they see. Many of the patients were exposed to organophosphates and they draw interesting parallels between the Gulf War veterans' bone changes and those they described in farm workers exposed to organophosphates. They also discuss other agents

given to the Gulf War veterans, such as pyridostigmine (they cite interesting data about the distribution of acetylcholinesterase in bone) and vaccinations, which might play a role in altered bone cell activity.

Others have examined the possible effects of mustard gas, which can be shown to have effects on haemopoietic stem cells in the bone marrow,<sup>3</sup> and of depleted uranium, which can lead to profound changes in osteoblasts, including a tumorigenic effect.<sup>4</sup>

This study is interesting because it raises the possibility of a specific disorder resulting from service in the Gulf War that is backed up by hard data. The authors are open about the possibility that the changes they see in bone might be as a result of the symptoms rather than their cause. However, when taken together with other data, there is an increasing body of evidence to indicate that service in the Gulf War has had, directly or indirectly, an effect on bone and suggests some possible mechanisms by which service in the Gulf War might have led to the bone cell dysfunction and subsequent bone loss that they observe.

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