

LETTERS TO THE EDITOR

Recent developments in the management of the pulmonary complications of HIV disease

The otherwise excellent article by Drs D M Mitchell and R F Miller (May 1992;47:381-90) seemed to be giving a mixed message so far as tuberculosis in the UK is concerned. At one point the authors say, "Although no increase has occurred yet in Britain . . .," yet in another place they state that notification of tuberculosis increased by 1.5% in 1988, and by 5.3% in 1989. In fact notifications of tuberculosis in England and Wales have increased successively in each year since 1987 with the exception of 1990. Uncorrected figures for the first quarter of 1992 show a considerable increase over the first quarter of 1991. As is shown in the accompanying figure, the increase in notifications in England and Wales now represents a considerable number of "unexpected" cases of tuberculosis, amounting to about 8 000 over six years. This figure is very similar to the increase in the United States, which has experienced a rise in notifications since 1985.

The authors quite rightly say that the rise in notifications of tuberculosis in the UK appears to have little relation to HIV infection. Analysis by age and sex¹ shows the increase to be predominately in the elderly, though an increase in younger females is also present.

The message that is implicit in the article but fails to be underlined is that tuberculosis notifications in the UK are increasing in parallel to the United States increase, yet without any indication that HIV is

implicated. When HIV eventually does affect tuberculosis in this country, as it surely will, the implications for the increase in tuberculosis could be very serious indeed.

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1 Nisar M, Narula S, Beeching N, Davies PDO. HIV related tuberculosis in England and Wales. *Tuberc Lung Dis* 1992;4:200-2.

Inhaled corticosteroids: benefits and risks

Dr D M Geddes (June 1992;47:404-7) has reviewed studies of the effect of inhaled corticosteroids on indices of bone metabolism, particularly osteocalcin. Unfortunately at least one potential mechanism of bone loss induction by inhaled corticosteroids has not been discussed. Suppression of adrenal androgen production may be a mechanism of bone loss, particularly in postmenopausal women. In particular, in table 2 Geddes states that Toogood¹ found "no detectable changes" relevant to bone metabolism. This is somewhat misleading, as Toogood did not measure osteocalcin or any direct indices of bone formation, turnover, or resorption. What Toogood did find was a highly significant suppression of dihydroepiandrosterone and androstenedione concentrations secondary to inhaled budesonide. This may be of considerable importance to the bone metabolism of postmenopausal women, who are critically dependent on such adrenal androgens as a substrate for peripheral conversion to oestrogen, and hence for some protection against loss of bone density.² A second possible mechanism of osteoporosis induced by inhaled corticosteroid, which has received little attention, is the effect of the swallowed portion of beclomethasone dipropionate on calcium absorption by the

gut. Ninety per cent of beclomethasone dipropionate from a metered dose inhaler is swallowed.³ On reaching the intestine beclomethasone dipropionate is activated to beclomethasone 17-monopropionate, which has far greater glucocorticoid effect than the parent drug.⁴ Beclomethasone 17-monopropionate is a stable product, is very sparingly soluble, and is poorly absorbed by the intestine.⁴ Thus a topical effect on gut calcium absorption could occur, given that reduction of calcium absorption is a known systemic effect of steroids, and a major mechanism of osteoporosis.⁵ We are currently assessing this possibility further.

Dr Geddes states that "the relation between low bone density and clinical events is uncertain." In fact, studies have shown a clear relation between bone density and fractures, finding an approximate doubling of fracture risk for each 10% of bone density loss.⁶ Thus bone density may be used as a valid measure of fracture risk in patients with asthma. In table 3 Dr Geddes reports that the study by Wolff⁷ found no change in bone density in five subjects receiving inhaled corticosteroids. In fact, these subjects had a mean hip bone density 10% below the predicted value, which failed to reach statistical significance only because of the extremely small sample size.

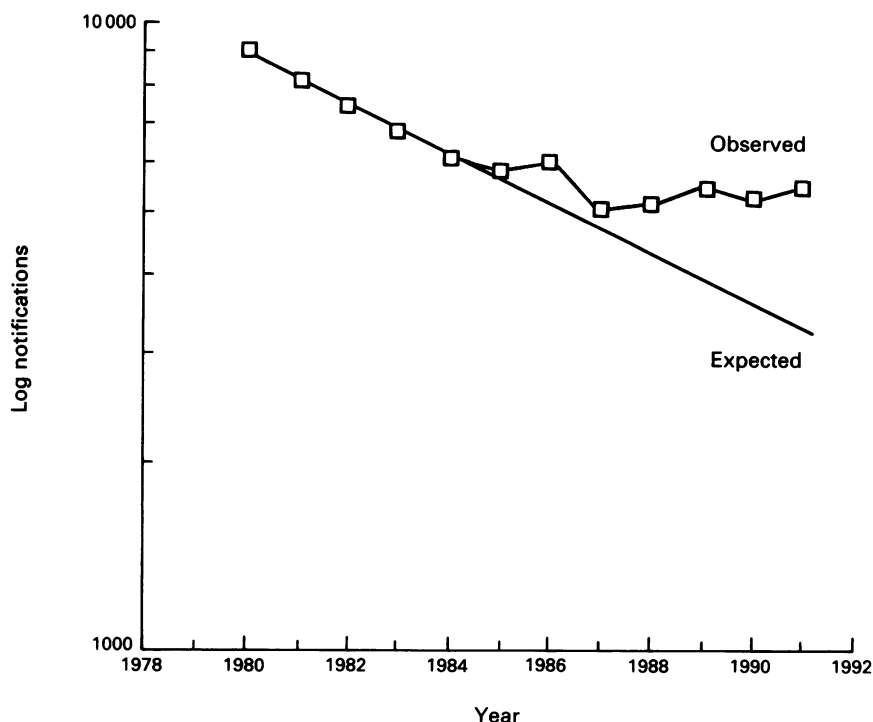
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Bone turnover during short course prednisolone treatment in patients with chronic obstructive airways disease

Despite the statement that patients with evidence of bone disease or any other important medical problems were excluded, one of the 10 patients in the study by Dr D Morrison and others (June 1992;47:418-20) had modestly increased calcium and parathyroid hormone (2.73 mmol/l and 8.5 pmol/l). This patient has primary hyperparathyroidism and should have been excluded from the study. Any patient with even a modestly raised calcium concentration should have undetectable parathyroid hormone. Does the patient have any symptoms?

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Total notifications of tuberculosis for England and Wales, 1980-91.