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The Editor of Tubercle
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27th November, 1982

Dear Sir,

Calcium metabolism during rifampicin and isoniazid therapy

Difficulties have arisen in deciding whether this compound treatment for tuberculosis has a significant clinical effect on calcium metabolism. Rifampicin given alone to normal Caucasian volunteers over a short interval caused a decrease in 25 hydroxycholecalciferol (25 HCC) but had no effect on calcium, immunoassayable parathyroid hormone or 1,25 dihydroxycholecalciferol (1). Isoniazid on the other hand significantly affected all these parameters (2). In our clinical series we were unable to establish an effect on serum calcium after six months combined treatment and furthermore the occurence of osteomalacia in 52 Indians followed could be simply attributed to their nutritional vitamin D deficiency (3). Only one European out of 31 in the series developed osteomalacia and this was due to a combination of low vitamin D intake and cirrhosis of the liver. Brodie and his colleagues have examined the effect of combined therapy and found only 25HCC levels were decreased at six months indicating that the effect was less than would have been predicted from the two drugs alone (4). However, using data from the BTA study (5) they did show a small but significant hypocalcaemic effect at six months (2). Serum albumin changes may have been sufficient to produce this difference or a bias of winter sampling for calcium in the second estimation. It should be noted that patients who were clearly hypocalcaemic in the BTA study were often Asian and were likely to be already suffering from osteomalacia before chemotherapy.

One case of suggested rifampicin induced osteomalacia has been reported (6). This female patient illustrates the difficulties. First the patient was taking ethambutol with rifampicin and thus a different pharmacokinetic situation existed compared with isoniazid. Second the patient was Indian and no estimation of vitamin D intake was made except the comment "milk and milk products were adequate" but unless fortified these have a negligible content of vitamin D. Not even in India can one assume that exposure to sunlight, especially in a female, is sufficient. Lastly a 25HCC level would at least have shown that the problem lay between intake or hepatic enzyme induction rather than other causes.

If rifampicin and isoniazid do have a clinical effect it is a small one for in relation to osteomalacia in Asians it is adequately overcome by 900 units of vitamin D_2 per day (3).

Yours	sincerel	y,

WAYNE PERRY, M.R.C.P.

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Abstract

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Calcium metabolism during rifampicin and isoniazid therapy.

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