Relationship between serum phosphate concentration and bone resorption in osteoporosis

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On the basis of quantitative evaluation of bone resorption in 26 patients with osteoporosis of unknown cause, a significant positive correlation was found between the level of resorption and the serum phosphate concentration. No such correlation was found with serum calcium concentration, bone formation, or alkaline phosphatase activity.

Irrespective of the cause of osteoporosis, the bone loss characteristic of this disorder is associated with an increase in the amount of bone resorption.[1] In some forms of osteoporosis, an increased concentration of phosphorus in the serum has been noted.[2-5] With the recent development of a new method for measuring the amount of bone resorption occurring in bone tissue at a particular time,[6] it became possible to search for a quantitative relationship between bone resorption and serum phosphorus concentration or other parameters of mineral metabolism in patients with osteoporosis.

Material and methods

Twenty-six patients were studied who had osteoporosis of unknown cause. No patient had received treatment. Roentgenographically, all but two had biconcavity of the intervertebral disks, and the majority had one or more fractures of vertebrae.

Serum calcium, phosphate, and alkaline phosphatase values were determined on samples taken while the patients were in the fasting state. Calcium was determined by semiautomated complexometric titration (normal values, 8.9 to 10.1 mg. per 100 ml.).[7] Phosphorus, as inorganic phosphate, was determined by the method of Gomori[8] (normal, 2.5 to 4.5 mg. per 100 ml.); and alkaline phosphatase activity was determined, in all but 3 patients, by the King and Armstrong method.[9] All patients had normal blood urea levels.

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At the same time the blood was sampled, a piece of bone was removed from the posterior iliac crest for quantitative microradiography.

The method of quantitative microradiography, as developed by Jowsey, allows a numerical evaluation to be made of the amount of resorption and formation taking place in a piece of bone tissue. In this method, sites where resorption and formation of tissue are taking place are identified in a microradiograph of a bone section. Bone resorption appears as a surface of high mineral density with an uneven surface; such an appearance has been correlated with the presence of osteoclasts (Fig. 1). Bone formation is characterized by low mineral density and has a smooth surface (Fig. 1); this appearance is found where osteoblasts and bands of osteoid tissue appear in the corresponding tissue section. The lengths of surfaces undergoing resorption and formation are measured and expressed as percentages of the total surface of bone in the section. These values, therefore, refer to the amount of surface occupied by the two aspects of bone turnover—bone formation and bone resorption; they will differ in different sites in a single skeleton but will bear relatively constant ratios to each other. Values for normal persons indicate that, for the range of ages of the patients included in this study, the values for resorption are between 2.2 and 8.3 per cent while the values for formation are between 1.7 and 3.9 per cent. Further details of this method and the results in both normal and osteoporotic individuals have been given elsewhere.[6]

The matrix of correlation coefficients for age, bone formation and resorption, serum calcium concentration, serum phosphate concentration, and serum alkaline phosphatase activity was obtained.

Results

None of the variables studied showed a significant correlation with age of the patient (Figs. 2 and 3 and Table I). Neither were any significant relationships found between bone formation and any of the variables measured. A significant positive correlation was found between bone resorption and serum phosphate values (Fig. 4). No significant relationships were found between resorption and serum calcium or alkaline phosphatase values.

Discussion

A relationship between patient's age and serum phosphate value has been demonstrated by Greenberg and co-workers[10] in normal females. That there was

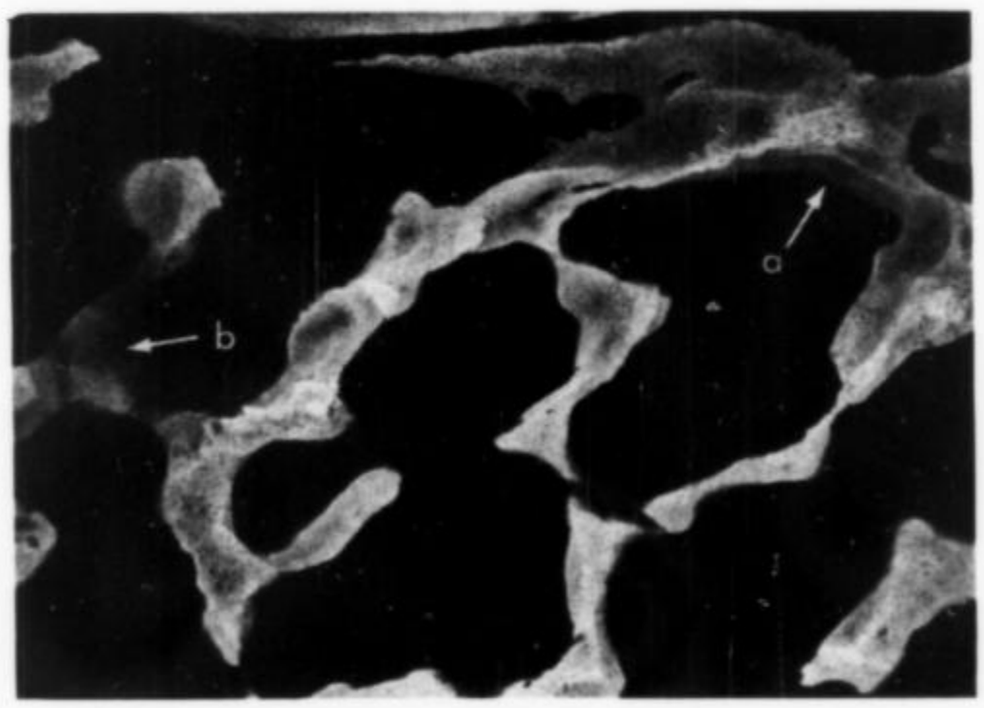

Fig. 1. a, Appearance of bone formation and *b,* bone resorption in microradiograph of trabecular bone (iliac crest). (Original magnification ×40.)

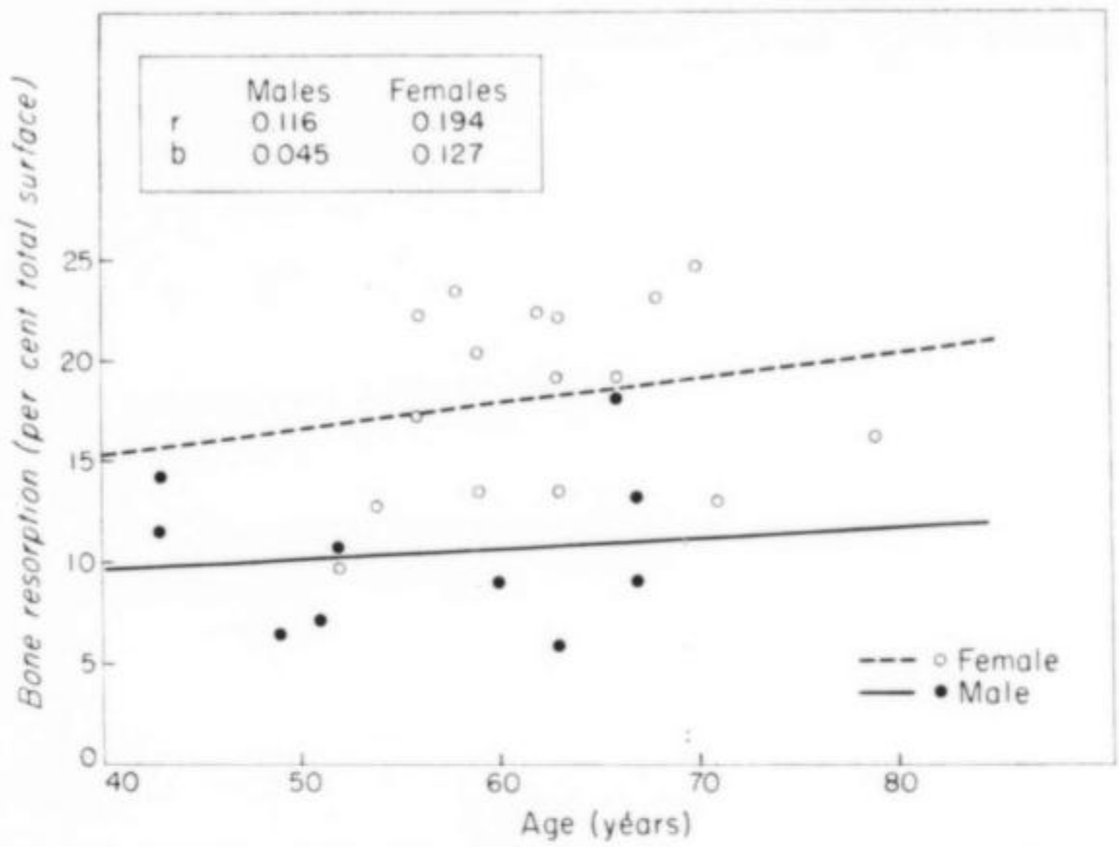

Fig. 2. Relationship between bone resorption and patient's age, showing no significant correlation.

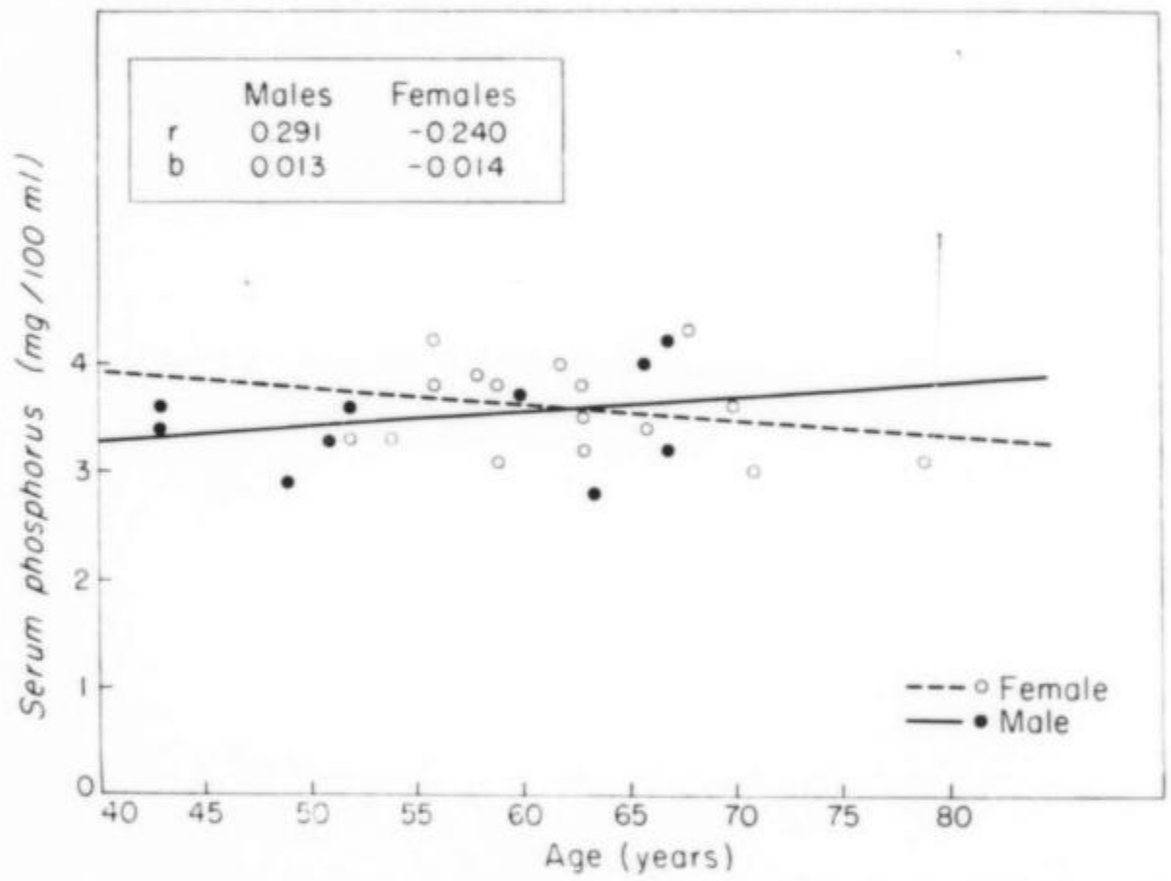

Fig. 3. Relationship between serum phosphate (shown as phosphorus) and patient's age, showing no significant correlation.

no such correlation in the osteoporotic patients considered here is not surprising because there is no reason to expect the activity of the disorder, as reflected by the serum phosphate level, to be related to age in osteoporotic patients.

The only positive relationship demonstrated by these data is the one between the serum phosphate and bone resorption values. We suggest that the basis of this relationship is suppression of parathyroid activity by high serum calcium levels.[11] If there is an increase in bone resorption because of an intrinsic abnormality of bone, or if bone in osteoporotic patients is more sensitive to parathyroid hormone, then the increased resorption of active osteoporosis would

Table I. Summary of data on osteoporotic patients

	X-ray findings		*Bone**		*Serum*		
Age (years)	*Fractured vertebrae (No.)*	*Biconcavity of disks*	*Resorption (%)*	*Formation (%)*	*Calcium†*	*Phosphate†*	*Alkaline phosphatase‡*
Females							
52	0	+	9.7	2.6	9.9	3.3	11.3
54	4	−	12.7	1.7	9.8	3.3	—
56	2	−	22.0	1.7	9.7	3.8	—
56	0	+	17.2	3.1	8.8	4.2	—
58	1	+	23.4	2.3	9.4	3.9	11.0
59	4	+	20.2	1.1	9.5	3.8	6.8
59	4	+	13.4	3.8	9.5	3.1	6.8
62	4	+	22.2	1.0	9.6	4.0	9.0
63	0	+	22.0	5.5	10.1	3.8	8.8
63	3	+	13.5	7.0	9.3	3.2	7.2
63	10	+	19.0	2.9	10.2	3.5	6.3
66	3	+	19.0	1.2	9.7	3.4	5.5
68	6	+	22.9	0.8	9.0	4.3	5.8
70	3	+	24.5	1.3	10.1	3.6	11.1
71	0	+	12.8	4.7	9.4	3.0	13.0
79	1	+	16.0	0.0	8.6	3.1	3.8
Males							
43	1	+	14.2	3.9	9.5	3.6	4.6
43	0	+	11.4	0.8	9.6	3.4	8.2
49	6	+	6.4	1.4	9.6	2.9	12.6
51	8	+	7.1	1.1	9.4	3.3	5.9
52	6	+	10.7	1.6	9.0	3.6	10.5
60	8	+	8.9	2.0	9.4	3.7	9.7
63	6	+	6.8	0.7	9.6	2.9	9.2
66	3	+	18.0	1.3	9.6	4.0	9.4
67	4	+	13.2	3.0	9.8	4.2	6.2
67	5	+	8.7	2.4	9.2	3.2	6.2

*These data reported as length of surface undergoing indicated change expressed as percentage of total length of surface in the section examined.
†As milligrams per 100 ml.
‡As King-Armstrong units per 100 ml.

release calcium and phosphate into the blood. The increase in calcium would suppress parathyroid activity and this, in turn, would increase renal tubular reabsorption of phosphate and result in a further increase in the serum phosphate level. Suppression of parathyroid activity may explain the observations that absorption of calcium by the gut is sometimes abnormally low in osteoporotic patients[12] and that excretion of calcium in the urine is increased.[13] Such an interpretation is supported by the fact that, in primary and surgically induced hypoparathyroidism, serum phosphate levels are higher than normal.[2] However, because increased serum calcium values are not characteristic of osteoporotic patients, parathyroid suppression in response to serum calcium levels is an unlikely explanation. Also, interpretation of serum phosphate levels in terms of parathyroid secretion is difficult, and, therefore, on the basis of the

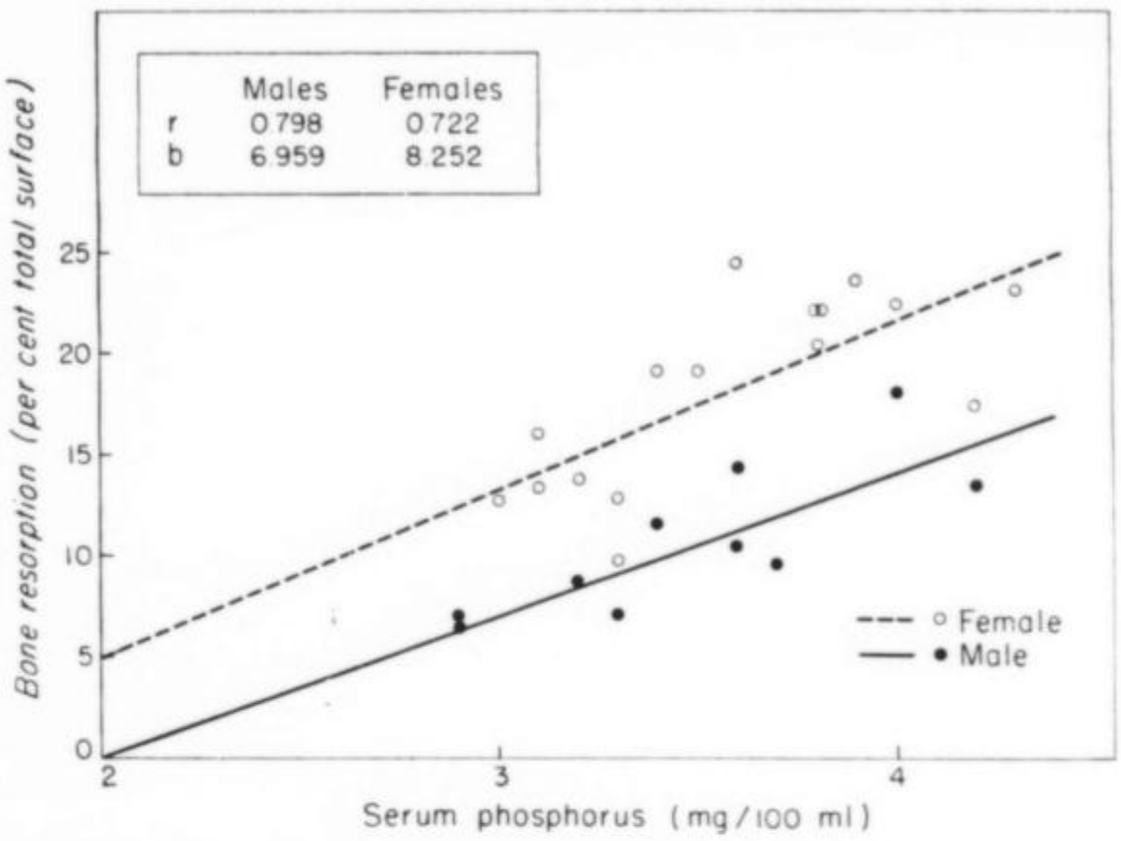

Fig. 4. Relationship between bone resorption and serum phosphate (shown as phosphorus); $P < 0.01$ for both correlation coefficients.

present data it is not possible to exclude other explanations. Further studies are necessary to evaluate such possibilities.

The data presented here demonstrate a relationship, not an over-all increase in serum phosphate levels. Heaney[3] and Whedon and Shorr[4] observed that serum phosphate values were higher in patients with acute disuse atrophy than in normal persons. In the present study on osteoporosis of unknown cause in ambulatory patients, the serum phosphate values were not higher than the accepted normal range in our laboratories. It may be that the level of bone resorption was higher in the patients with acute disuse atrophy than in osteoporosis.

Regardless of the pathogenic mechanism involved, the empiric observation that the serum phosphate concentration correlates positively with the level of bone resorption may be useful in estimating the level of bone resorption in untreated osteoporotic patients and, therefore, the severity of the disease.

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