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## Bone Marrow Acid Phosphatase in the Evaluation of Patients with Carcinoma of the Prostate

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*Based on experience with 30 men having clinical stage A and B adenocarcinoma of the prostate, the authors conclude that elevation of bone marrow acid phosphatase (BMAP) is a sensitive indicator of the disease state. BMAP revealed periprostatic or nodal involvement when osseous metastases seemed absent. BMAP is considered essential in the evaluation of all patients with prostatic carcinoma. Patients who have false negative BMAP (and are not candidates for radical prostatectomy), should undergo lymphangiography and bone scan before radiation therapy or hormonal treatment is planned.*

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Recent studies <sup>1-7</sup> have indicated that elevation of acid phosphatase activity in bone marrow aspirate may be the earliest indication of advanced carcinoma of the prostate (stages C and D). Elevation of bone marrow acid phosphatase (BMAP) frequently reveals abnormality before other techniques employed in staging prostatic carcinoma, such as digital palpation of the gland, serum acid phosphatase, skeletal metastatic survey, bone scan and lymphangiography. BMAP, therefore, is an essential part of the workup of all patients with prostatic carcinoma. Its measurement may be critical in determining the stage of the disease and appropriate treatment, eg: radical surgery, radiation therapy or hormonal manipulation.

### Materials and methods

Thirty men with clinical stage A and B adenocarcinoma of the prostate were studied. Their ages ranged from 49 to 75 years. Each patient underwent complete evaluation including serum acid and alkaline phosphatase, skeletal metastatic survey, bone scan, lymphangiography and BMAP determination.

The technique of lymphangiography and its interpretation in patients with carcinoma of the prostate has been reported.<sup>3</sup>

BMAP was obtained by atraumatic aspiration of 5 cc of bone marrow from the posterior iliac crest. This site was chosen in preference to the sternum because of the known free communication of periprostatic, pelvic and paravertebral veins with the marrow space of the iliac crest. At the time of marrow aspiration, a blood sample was drawn and the specimens delivered immediately to the laboratory. Because of instability of the enzyme, analyses for acid phosphatase were performed within 30 minutes of their receipt in the laboratory. Acid phosphatase activity was measured by the Roy method (thymolphosphaline phosphate), as modified for the Dupont ACA.<sup>8</sup> This method has great specificity for prostatic acid phosphatase and minimizes the contribution of acid phosphatase of marrow cellular, eg: RBC, platelet, origin. Normal range for both serum and marrow acid phosphatase by this method is 0-0.7 I.U.

## Results

Fifteen patients (Group I), in whom staging studies failed to demonstrate distant metastases, underwent radical retropubic prostatectomy and lymphadenectomy including the sacral, obturator, hypogastric, external iliac and common iliac nodal drainage to the aortic bifurcation. The remaining 15 patients (Group II) were found to have stage D disease. Seven of these patients received irradiation therapy to the prostate and its nodal drainage, and eight underwent treatment by hormonal manipulation.

In 11 of 15 patients in Group I (73%), neoplasm was found to have extended beyond the confines of the prostatic capsule. Carcinoma was found in the regional lymphatics in six patients, the periprostatic tissues in four and seminal vesicles in one. Elevation of BMAP (range .90-2.0 I.U.; mean 1.2 I.U.),

was noted in 10 of the 11 patients (91%) only three of whom had elevation of serum acid phosphatase. One of the 11 patients with extraprostatic carcinoma had normal BMAP and serum acid phosphatase levels. Of four patients with the neoplasm confined to the prostate gland, one had deviation of BMAP and all had normal serum acid phosphatase.

Of the 15 patients in Group II with stage D carcinoma of the prostate, 13 (87%) had elevated BMAP (range .80-7.2 I.U.; mean 1.9 I.U.). Four of these also had elevated serum acid phosphatase. In nine patients, this study was normal. Both patients with stage D disease and normal BMAP had normal serum enzyme levels.

Other staging studies and their diagnostic accuracy in demonstrating advanced (stage C and D) disease were lymphangiography 55%, bone scan 55%, plasma acid phosphatase 23% and bone survey 14%.

## Discussion

The accuracy of BMAP in predicting neoplastic dissemination in patients with carcinoma of the prostate, and its superiority to other staging techniques routinely used in this disease, were underscored in this study. Thus, of 11 patients found to have local and lymphatic extension at the time of operation, 10 (91%) had elevated BMAP. Three of four operated patients in whom the carcinoma was confined to the prostate gland had normal BMAP (75%) and one patient had false positive elevation. Similarly, in 15 patients with demonstrated stage D metastatic disease, BMAP was elevated in 13 (87%).

As described, other frequently employed staging studies were less accurate in predicting extent of the carcinoma, with bone scan and lymphangiography demonstrating met-

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astases in 55% of patients, and elevation of serum acid phosphatase and abnormal bone survey indicating advanced disease in 23% and 14%, respectively. These findings do not obviate the need for these staging techniques, but suggest they be employed to corroborate BMAP, define the exact location of metastases when BMAP is elevated and to demonstrate, when possible, metastatic carcinoma of the prostate in those rare instances when BMAP is incorrect.

The exact mechanism for elevation of BMAP is not clear. Probably one or both of two mechanisms are responsible for elevation of this enzyme in the bone marrow, while plasma levels remain normal. First, it is possible that in those patients with normal bone survey and scan, and only locally demonstrated periprostatic tumor extension, there are in fact microscopic foci of neoplasm in the bone marrow, which will later become clinically apparent. Second, the extensive and free communication of peri-

prostatic, pelvic and paravertebral veins with the marrow space of the iliac crest suggests that high concentrations of acid phosphatase may be delivered to bone marrow for some time prior to equilibration with the systemic circulation. Long term follow-up of this group of patients will ultimately substantiate or refute this mechanism.

### Summary

It is concluded that (a) BMAP is the most sensitive indicator of stage C and D carcinoma of the prostate, (b) BMAP is capable of indicating periprostatic or nodal involvement in the apparent absence of osseous metastases, (c) lymphangiography and bone scan are of especial value in patients with false negative BMAP, and in planning radiation therapy or hormonal manipulation in patients who are not candidates for radical surgery.

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