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Changes in Serum Testosterone after Bilateral Orchiectomy in Patients with Metastatic Carcinoma of the Prostate

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From a study of 38 patients, it may be concluded that, first, changes in serum testosterone levels of patients undergoing orchiectomy for metastatic carcinoma of the prostate are unrelated to the clinical course of the patient; second, no clear correlation exists between quantitative Leydig cell counts and levels of plasma testosterone; and, third, exacerbation of metastatic disease is observed while plasma testosterone remains in the castrate range. These observations question the exact function of the Leydig cell and its role in androgen production, and indicate that prostatic neoplasms have varying degrees of response to reduced androgen levels and/or androgen-like substances following castration.

Hormonal treatment of patients with metastatic prostatic carcinoma has been directed at lowering androgen production by the testes. Generally, this decrease in androgen production has been assessed by measurement of total urinary 17-keto steroid and/or individual urinary androgen metabolites. Recent studies indicate that such determinations are of limited value since the steroids measured are derived from both adrenal and gonadal precursors, some of which are weakly androgenic, or even nonandrogenic.

Plasma testosterone measurement offers a more direct approach to the study of tumor androgen relationships since it is the most potent androgen secreted. Seventy percent of testosterone measured in plasma in men arises from the testes. The present study was designed to evaluate the relationship of plasma testosterone levels to the clinical response of patients undergoing bilateral orchiectomy for metastatic carcinoma of the prostate.

Materials and methods

Thirty-eight men with proven carcinoma of the prostate and symptomatic bony metastases were treated with bilateral therapeutic orchiectomy. Immediate preoperative and three-day postoperative serum testosterone levels were determined. Correlations were made between a) preoperative testosterone levels, b) fall in postoperative testosterone...
levels, c) acid and alkaline phosphatase, d) testicular-Leydig cell counts, and e) presence or absence and length of clinical symptomatic improvement.

Quantitative Leydig cell determinations were made by counting the actual number of Leydig cells and seminiferous tubules in 100 random fields of each testis, then averaging the number of Leydig cells per seminiferous tubule.

The method of plasma testosterone determination is that modified from Kato and Hortens, utilizing competitive protein binding.

**Results**

Plasma testosterone, measured mug/100/ ml plasma, ranged from 110 to 1404 (mean 506), prior to orchiectomy, and fell from 12 to 187 (mean 64), postoperatively. The average postoperative testosterone determination was 15% of its preoperative level.

Plasma acid phosphatase, measured in King-Armstrong units, ranged from 4 to 317 (mean 39), prior to orchiectomy, and fell to from 2 to 54 (mean 10), postoperatively. The average postoperative acid phosphatase was 25% of its preoperative level.

Leydig cell counts, eg, number of Leydig cells per seminiferous tubule, showed gradual reduction with increasing patient age. Average number of Leydig cells was seven in the age group 30-39, and decreased to three in the age group 65-75.

Thirty-six of 38 patients undergoing orchiectomy noted immediate relief of osseous pain. Within six months of operation, however, 32 of the 36 noted recurrence of varying degrees of pain, as well as other stigmata of metastatic disease.

No significant correlation was observed between (a) preoperative testosterone levels and Leydig cell counts, (b) ratio of postoperative/preoperative testosterone and degree and duration of remission of symptoms, (c) ratio of postoperative/preoperative acid phosphatase and degree of duration of remission of symptoms, or (d) clinical response in patients having well differentiated vs poorly differentiated adenocarcinoma of the prostate.

Clinical exacerbation of metastases following initial remission, manifested by recurrent pain, progressive osseous involvement and increasing levels of acid phosphatase activity, was not accompanied by increase in plasma testosterone, which remained in the castrate range.

**Discussion and Conclusion**

It was distressing to observe that while 36 of 38 patients had excellent immediate relief of metastatic pain following orchiectomy, all but four noted varying degrees of recurrence within six months postoperatively. While prompt decrease in plasma testosterone followed orchiectomy, that decrease was neither related to Leydig cell counts or degree and duration of remission of symptoms. Of further interest was the observation that plasma testosterone remained in the castrate range in the face of recurrent activity of the neoplasm, and response to orchiectomy was unrelated to tumor grade.

The poor response to orchiectomy seen in many patients may represent a) a marginal and transient tumor androgen dependence, b) hypersensitivity to minute amounts of adrenal androgen, eg, androstanedione which is convertible to testosterone, or c) nonandrogenic factors stimulating the neoplasm.