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Letter to the Editor

Hormone Levels in Prostatic Fluid from Healthy Finns and Prostate Cancer Patients*

DAVID P. ROSE,†‡ KRISTIINA LAAKSO,§ MARTTI SOTARAUTA¶ and ERNST L. WYNDER§
Divisions of ‡Nutrition and Endocrinology and §Epidemiology, Mahoney Institute, American Health Foundation, New York, U.S.A. and ¶University Hospital of Kuopio, Finland

WHILE it is generally believed that endocrine factors are important in the etiology of prostate cancer, plasma hormone assays have failed to demonstrate any unequivocable abnormality [1]. For example, although therapeutic response to orchidectomy and antiandrogens suggests the involvement of testosterone, plasma levels in prostate cancer patients have been variously reported as normal [2, 3], elevated [4, 5] and subnormal [6].

Prostatic fluid is a secretory product of the merocrine and apocrine cellular components of the prostate, and as such is likely to reflect metabolic activity and the microenvironment within the gland [7]. While a number of biochemical constituents of prostatic fluid have been studied, and abnormalities described in prostate cancer [8, 9], data do not appear to have been published dealing with its hormone content. In the present study prostatic fluid and serum estradiol (E_2), estrone (E_1), testosterone (T) and prolactin (PRL) levels were assayed in untreated prostate cancer patients, and compared with those of healthy volunteers of similar age (mean age ± S.D.: 70 ± 7 and 66 ± 10 yr respectively). All were residents of rural Kuopio County, Finland.

Prostatic fluid, 100–200 μl, was obtained by transrectal massage and, together with a corresponding serum sample, stored at −20°C prior to air shipment to New York in insulated containers packed in dry ice. Serum and prostatic fluid T were determined by radioimmunoassay using kits purchased from Immunochem Corp. (Carson, CA). The interassay coefficient of variation as determined in our laboratory was 8.2%, and the sensitivity 20 ng/100 ml. Radioimmunoassays of E_1 and E_2 were performed by a subtraction method with reagents obtained from Radioassay Systems, Inc., Carson, CA; the interassay coefficient of variation for total estrogens was 6.2%, with a sensitivity of 5 pg/ml, and for E_2, 6.4%. Prolactin was measured by a double antibody radioimmunoassay technique which had an interassay coefficient of variation of 4.3%, with a sensitivity of 1 ng/ml.

Neither the serum nor prostatic fluid concentrations were distributed normally in either the prostate cancer or control groups. For statistical analysis, serum and prostatic fluid hormone assay results were converted to $\log_{10}$ prior to evaluation by Student's t test. For purposes of comparison, the upper limits of normal were defined as the mean control value +2 S.D.

The individual results for prostatic fluid E_2 and E_1 are shown in Fig. 1, together with the mean ± S.D., which reflects the wide variation in values. Nevertheless, the E_2 concentrations were clearly higher in prostatic fluids from prostate cancer patients compared with controls ($P<0.001$), whereas the E_1 concentrations were not significantly different. Serum E_1 and E_2 levels (Table 1) were similar in the cancer patients and controls, and were frequently lower than the corresponding prostatic fluid values. For the controls, 10/34 (29%) of the prostatic fluid E_2, and 10/33 (30%) of the E_1 levels were above the serum means + 2 S.D. This concentration of estrogens into prostatic fluid was even more pronounced in the cancer

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‡To whom correspondence should be addressed at: American Health Foundation, 320 E. 43rd Street, New York, NY 10017, U.S.A.

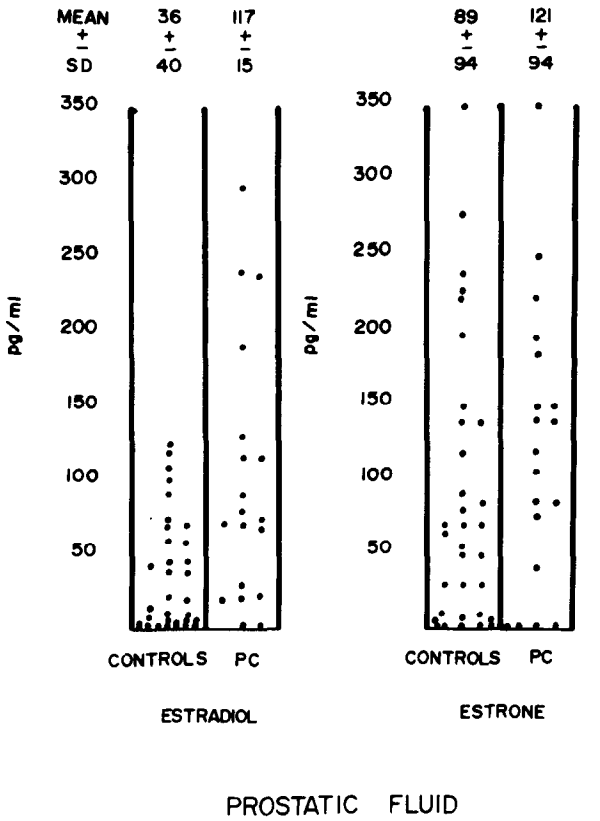

Fig. 1. Estradiol and estrone levels in prostatic fluid from prostate cancer patients (PC) and healthy controls of similar age.

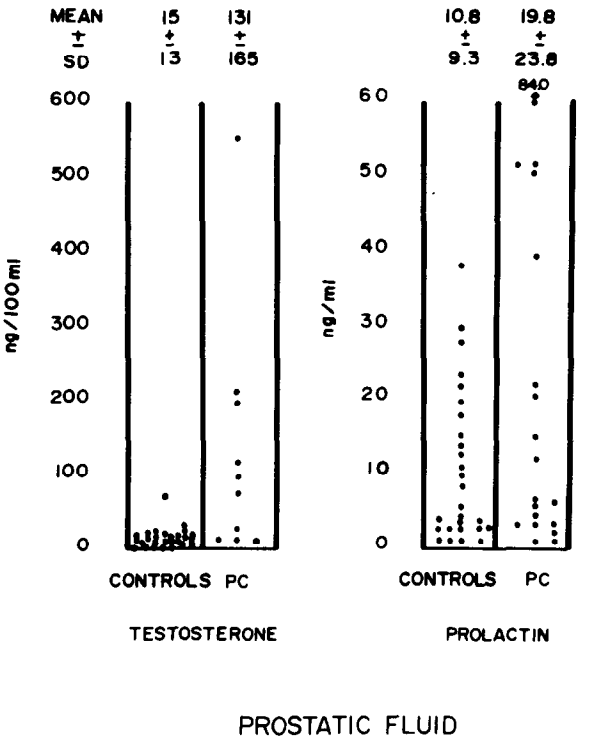

Fig. 2. Testosterone and prolactin levels in prostatic fluid from prostate cancer patients (PC) and healthy controls of similar age.

patients: 13/20 (65%) of the E_2 and 10/20 (50%) of the E_1 levels were greater than the serum means + S.D.

The volumes obtained were sufficient to perform prostatic fluid T assays on samples from only 28 controls and 10 cancer patients (Fig. 2). The results were extremely low in the controls compared with their serum levels, all being <70 ng/100 ml ($P<0.001$). In contrast, 6 of the fluids from prostate cancer patients contained high concentrations of T, ranging from 73 to 550 ng/ml. Results for prostatic fluid PRL assays were available from 27 controls and 19 patients. Although there was no statistically significant difference between the groups, 5 of the cancer patients (26%) had elevated prostatic fluid, but normal serum levels.

We have demonstrated for the first time that both steroid and peptide hormones are present in prostatic fluid, and that they may occur at concentrations higher than those in serum. Several factors may influence the hormone content of prostatic fluid, including the circulating levels available for uptake by the gland, the degree of tissue binding, steroid-metabolizing activity of prostatic cells and, perhaps, the capacity for internalization of membrane-bound PRL.

There is no ready explanation as to why E_2 appeared to concentrate preferentially in the fluids of the prostate cancer patients. One possibility is that enhanced uptake of E_2 occurs in some cancerous glands because the tumor cells possess high concentrations of receptors which selectively bind this estrogen [10]. The most likely explanation for the extremely low prostatic fluid T levels in the controls is that they reflect the proportion of the serum steroid which is not

Table 1. Serum hormone levels (mean ± S.D.) in prostatic cancer patients and healthy controls

Group	Estradiol (pg/ml)	Estrone (pg/ml)	Testoterone (ng/100 ml)	Prolactin (ng/ml)
Controls	35 ± 12 (34)*	54 ± 25 (34)	537 ± 186 (28)	4.9 ± 3.9 (34)
Prostate cancer	32 ± 16 (20)	53 ± 27 (20)	344 ± 235 (10)	6.8 ± 4.6 (20)

*No. of subjects shown in parentheses.

bound to sex hormone-binding globulin, plus high tissue 5α-reductase activity with conversion of T to dihydrotestosterone.

In conclusion, the present results, although preliminary, suggest a novel approach to the study of prostate endocrinology, and one which is more likely to reflect hormonal events within the gland than assays of serum samples.

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