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Biochemical and Morphologic Studies of the Prostate Gland in Men Subjected to Radical Cystectomy

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ABSTRACT

Whole human prostate glands obtained from patients undergoing radical cystectomy were dissected into three paired lobes and the various parts of the gland were subjected to biochemical and morphologic examination. No distinct differences were found between the prostate lobes in regard to content of divalent cations, acid phosphatase and ATPase. These findings were concordant with observations at light microscopy. Hence, despite discernible change in cellular appearance, no distinct border was observed between lobes indicating separate "compartments"

INTRODUCTION

Acid phosphatase, Zn^{2+} and Mg^{2+} are well known secretory products in human seminal plasma (4,5,6,9). An Mg^{2+} and Ca^{2+}-dependent ATPase system was found to be another important seminal component (10). Studies of split ejaculate revealed all these parameters to be part of the human prostatic secretion (1,10). In further analyses this ATPase activity was found to be associated with the presence of organelles in the seminal plasma (10).

The aim of this study was to clarify more thoroughly the extent to which these organelles, later denoted prostasomes (2,12), and also the other substances, are present in and excreted from the human prostatic gland, and whether local differences with regard to content of these substances exist in different parts of the prostate.

MATERIAL AND METHODS

Prostatic tissue was obtained from seven men aged 59 - 68 years who were undergoing radical cystectomy, including total prostatectomy, because of bladder cancer. None of the men had had symptoms or signs of prostatic disease before

the operation. All had received preoperative irradiation to a dosage of 40 Gy over 3 weeks, and cystectomy and urinary diversion were performed 3 weeks after termination of radiotherapy. Immediately after the operation the prostatic gland was dissected free from the bladder, the seminal vesicles and adhering tissues.

The prostate was then further dissected into three paired lobes as described by Tissell & Salander in 1975 (13). In three of the seven cases the prostatic tissue was immediately prefixed in isotonic glutaraldehyde (3 %) buffer solution (280 mosmol/l), kept at $4^{o}C$ until fixation for electron microscopy with osmium tetroxide, and embedded in epon according to Ronquist et al. (10). In the other four cases all the material was immediately stored in a moist chamber at $0^{o}C$ and kept in a solution of ice and water to maintain temperature stability. After 4 to 7 hours representative specimens of prostatic tissue were carefully cut from this material and prefixed in glutaraldehyde for electron microscopy as outlined above. From the remaining prostatic cut sections, secretory fluid was gently squeezed from the ductules and collected in small plastic tubes. The fluid was diluted 1:3 with 0.15 M NaCl solution and centrifuged at 2 000 x g for 10 minutes. The residual pellet, containing cells and cell debris, was discarded and the supernatant was used for biochemical analyses.

Magnesium, calcium and zinc were determined in an atomic absorption emission spectrophotometer. Acid phosphatase was measured colorimetrically according to a tartrate-inhibition method (7). Mg^{2+}- and Ca^{2+}-dependent ATPase activity was measured according to Ronquist et al. (10). The protein concentration was measured with the method of Lowry et al. (8). To avoid influence of possible external fluid on concentration, the parameters were related to the protein concentration of the fluid.

In three patients the prostatic dissection disclosed well-defined periurethral hyperplastic nodules, the largest with a diameter of 20 mm. The nodules were removed from the prostatic tissue without rupture of the surrounding capsule. The solitary nodules likewise were sectioned for electron microscopy. Moreover, secretion was obtained by gentle squeezing for the aforementioned biochemical investigations. No contamination with prostatic tissue material was possible, as the nodules were separately prepared.

RESULTS

Biochemical investigations

The values for acid phosphatase, calcium, magnesium and zinc were as expected for prostatic fluid, although the analyzed specimens were obtained from squeezing of the dissected glandular material (Table 1). In all cases the Mg^{2+}-

and Ca^{2}-dependent ATPase activity could readily be recorded and was present at a level higher than that expected for mixed seminal plasma (containing secretion also from seminal vesicles, testes and epididymes). The hyperplastic nodules displayed essentially the same content of these substances as the prostatic tissue.

Table 1. ATPase, acid phosphatase (AP), calcium (Ca), magnesium (Mg) and zinc (Zn) in fluid from the prostate gland in 4 men and in adenomatous tissue from 3 of the same glands

	ATPase (nmol x min^{-1} x g $protein^{-1}$)	AP (μkat x g $protein^{-1}$)	Ca	Mg	Zn
			(μmol x g $protein^{-1}$)		
Prostatic gland					
mean	54.5	235	171	44.4	21.0
SDn^{-1}	41.3	197	111	17.1	12.0
range	8.2-170	59.0-684	72.2-396	24.8-68.0	7.9-47.0
Hyperplastic nodules					
mean	50.1	129.3	135	54.2	21.6
SDn^{-1}	16.5	53.5	48.7	29.6	5.3
range	38.8-69.0	91.0-190	98.6-190	34.8-88.3	16.3-26.9

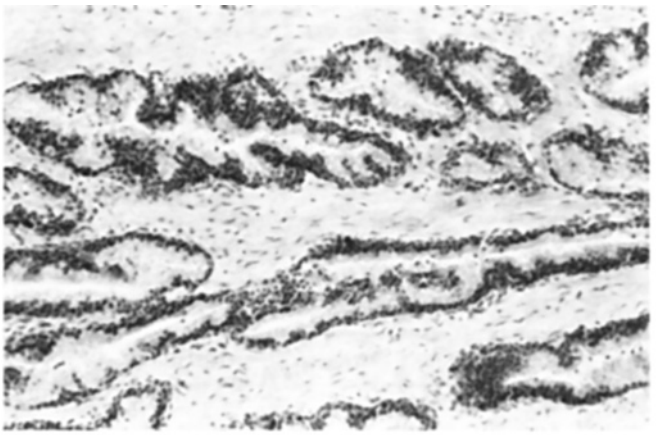
The concentration of these substances varied to some extent within different prostatic lobes, but without statistically significant differences (Table 2). Nor was any mutual correlation found between the parameters with different locations in the gland.

Table 2. Values for prostatic fluid according to lobe of origin [abbreviations as in Table 1. Means (SDn-1)]

Lobes from 4 glands	ATPase	AP	Ca	Mg	Zn
Dorsal	40.9 (24.3)	258.9 (212.9)	178.0 (101.8)	44.1 (20.8)	23.2 (12.6)
Lateral	75.7 (64.1)	298.0 (269.0)	144.0 (114.0)	40.1 (11.1)	21.9 (17.5)
Medial	42.0 (15.1)	149.0 (95.2)	192.0 (141.0)	49.1 (21.4)	17.8 (6.2)

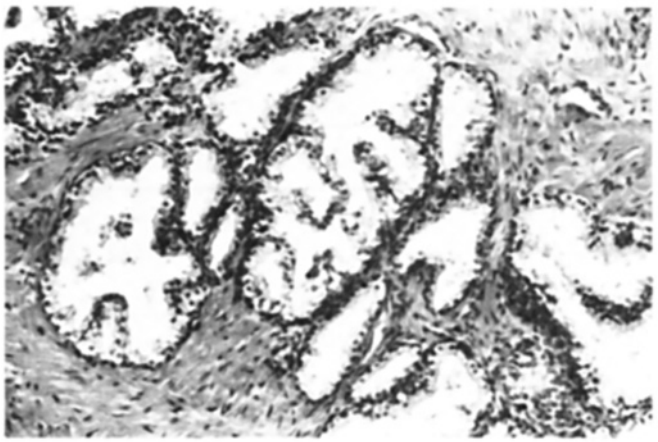
Fructose was not detected in any of these fluid specimens from the prostate gland.

Fig.1



A. Section showing the dorsal lobe pattern. Acini arranged in a parallel pattern with simple papillary projections (original magnification x 41).

B. Lateral lobe pattern with irregular acini and coarse stroma. Note the mild inflammatory changes and sloughing of the glandular epithelium, probably due to the preoperative irradiation (x 41).



C. Medial lobe pattern with prominent papillary formations (x 41).

Light microscopy

The morphologic pattern within each isolated lobe was generally variable (Fig. 1), i.e. did not show purely medial, lateral or dorsal lobe characteristics as described by earlier authors (11). In two cases, however, pure patterns were observed, one with a typical dorsal lobe pattern and another with a typical lateral one.

Transmission electron microscopy

Fig. 2 shows the intracellular location of prostasomes within other, bigger organelles, the storage vesicles. Very few, if any, prostasomes are free in the cytoplasm (2). The size and general appearance of the intracellular prostasomes are the same as in prostasomes isolated from prostatic fluid and seminal plasma (2).

DISCUSSION

The patients from whom the tissue material was obtained had been irradiated preoperatively because of bladder cancer. As the radiotherapy was directed not only towards the bladder, but also to the pelvic lymph nodes, shedding irradiation could have involved the prostatic tissue used in our investigations. The registered biochemical values thus may have been lower than in nonirradiated men, but this did not seem to be the case. Ultrastructural, atrophic changes may also be expected after radiotherapy.

In the present study there were no distinct differences between the prostate lobes in regard to their content of divalent cations, acid phosphatase and ATPase. Convincing evidence has accumulated that this latter enzyme system is intimately linked to the enveloping membrane of organelles (prostasomes) occurring free in prostatic fluid and seminal plasma (10) as well as in prostatic tissue (secretory cells and acinar ducts, cf reference 2 and Fig. 2). The ATPase activity may function as a quantitative measure of the presence of prostasomes. These findings were concordant with the observations at light microscopy. Hence, although a change in cellular appearance was discernible, no distinct boundaries were observed between lobes that could indicate "compartments".

Our study also indicated similarities between hyperplastic and normal prostatic tissue, although the hyperplastic tissue did not macroscopically present ducts connecting with other prostatic ducts. Earlier authors (14) showed that the zinc content/g tissue was at least equal in hyperplastic and normal prostatic tissue. In our cases, moreover, the hyperplastic nodules were enveloped in a fibrous capsule. This investigation supports the view that hyperplastic tissue may develop from obstructed parts of the true prostatic gland, because of the demonstrated similarities between the two tissue types.

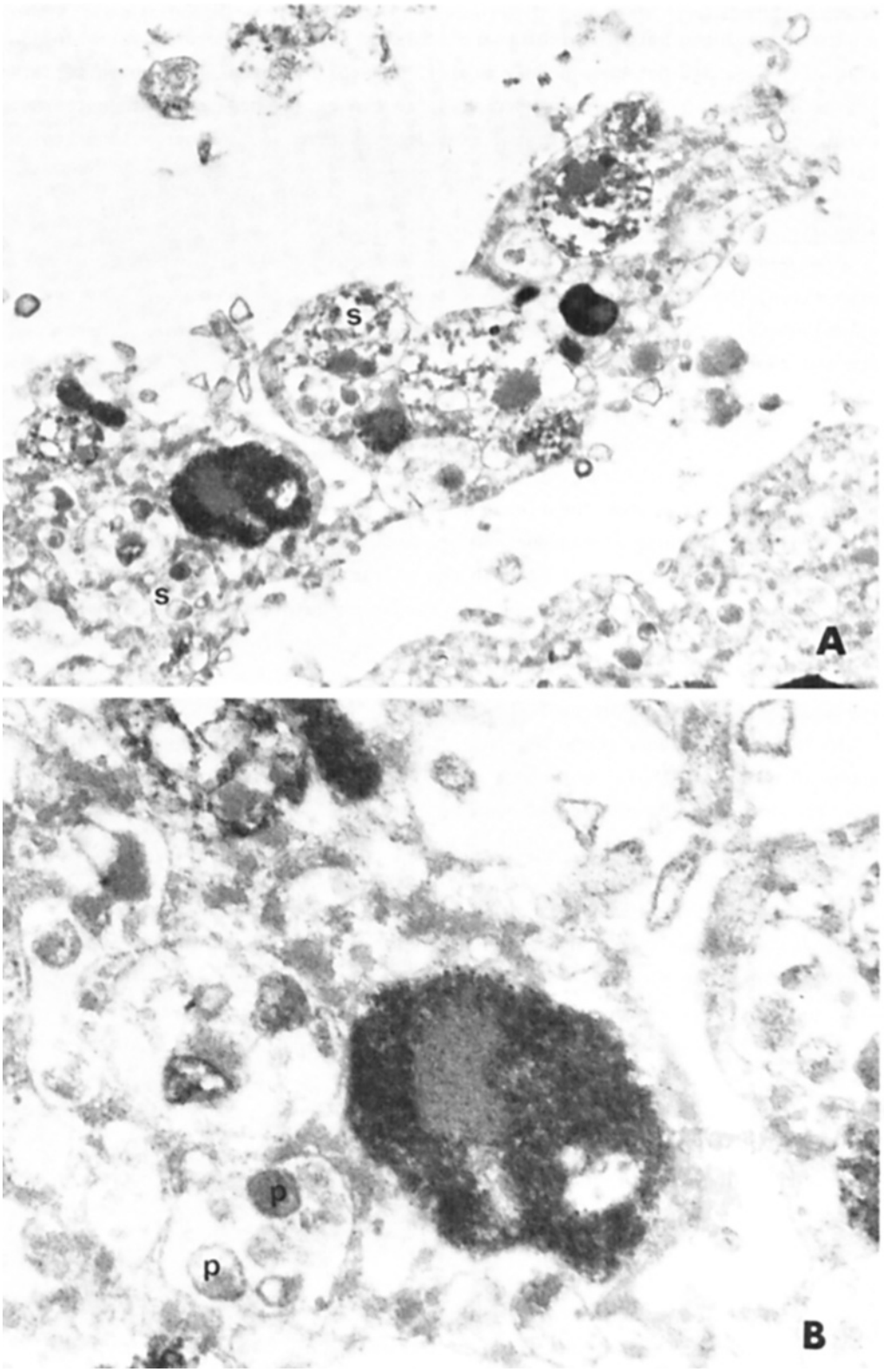

s
s
A
p
p
B

Fig. 2
A. Storage vesicles (S) in epithelial prostatic cells. The storage vesicles containing prostasomes are encased in a trilaminar membrane (x 27 000)
B. Higher magnification of membraneenveloped prostasomes (p) in storage vesicles (x 67 000)

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