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A histoquantitative study on the effects of castration on the rat ventral prostate lobe*

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INTRODUCTION

The light microscopical sequelae of castration on the rat ventral prostate are well documented (Moore, Price & Gallagher, 1930; Korenchevsky & Dennison, 1935; Price & Williams-Ashman, 1961; Aumüller, 1979). Within a few days of castration, the prostatic epithelium decreases, the glandular acini shrink, and the proportion of stroma appears to increase (Moore *et al.* 1930). It is noteworthy, however, that all the histological investigations have been descriptive or qualitative in nature, which has made it difficult to evaluate the quantitative changes of, e.g. epithelium and stroma, during tissue atrophy. The study of Arvola (1961), on the hormonal control of the amounts of the prostatic tissue components, is a notable exception in this respect.

Quite recently, new stereologic morphometrical or histoquantitative methods have been applied successfully to studies on the prostate gland. Bartsch (1977) and Bartsch & Rohr (1977) have developed stereologic morphometrical methods to be used at both light and electron microscopical levels and the study of human prostate has been especially emphasized (Bartsch *et al.* 1979*a*, *b*). DeKlerk & Coffey (1978) have been able, by the use of so-called biomorphometrics, to determine the total number of stromal and epithelial cells of the prostate, from which has resulted the important differentiation between prostatic hyperplasia (increase in cell number) and hypertrophy (increase in cell size). We have been able to introduce an improved histoquantitative method for the study of rat ventral prostate (Romppanen, Huttunen & Helminen, 1980) so that such parameters as surface and length densities of the glandular tubules, mean free distance between glandular tubules, and diameter of the glandular tubules have been calculated. The above mentioned methods provide an opportunity to carry out morphometrical (quantitative histological analysis of fixed tissue sections) studies on prostatic tissue which have not been possible hitherto.

Until recently, the epithelium of the prostate has been regarded as the main and possibly only target of androgenic hormones in the prostate gland (cf. Aumüller, 1979). During the last few years, however, increasing attention has been paid to the role of the stroma in the regulation of the differentiation of the prostatic epithelium (Franks, Riddle, Carbonell & Gey, 1970; Cunha, 1973; DeKlerk & Scott, 1978; Müntzing, Liljekvist & Murphy, 1979). The aim of the present study was to determine, using a new histoquantitative method (Romppanen *et al.* 1980), the effects

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of castration on the various stereologic morphometrical parameters of the rat ventral prostate. It was thought possible to achieve, by this means, a deeper quantitative insight into the involvement of the epithelial and stromal tissue compartments in hormone-induced tissue atrophy.

MATERIALS AND METHODS

Experimental animals and preparation of the tissue

Adult male rats of the Wistar strain were used. By weight the rats made up a quite homogeneous group (Table 1). Altogether, 63 rats were used; 38 rats were castrated, while 25 animals served as controls (Table 1). The rats were exsanguinated during ether anaesthesia. The ventral prostate lobes were carefully dissected free, weighed in a torsion balance (United, N.V. Vereenigde Draadfabrieken, Nijmegen, Holland), and fixed in 10 % formalin (buffered to pH 7·4) for 48 hours at 4 °C. From paraffin-embedded tissue blocks, 5 μm thick sections were cut and, subsequently, stained according to van Gieson's method for collagen fibres (Luna, 1968). One section of each ventral lobe was cut at about the level of the largest circumference of the lobe. As shown elsewhere (Romppanen *et al.* 1980), the two sections were representative for the whole ventral prostate.

Morphometrical-stereologic method

(1) *Stereologic model of the rat ventral prostate*

The ventral lobe of the rat prostate has been said to consist of rod-like or cylindrical, folded, and occasionally branching tubules, which are embedded in connective tissue (Aumüller, 1979; Price & Williams-Ashman, 1961). We have recently shown that glandular tubules of rat ventral prostate are quite randomly oriented and homogeneously distributed (Romppanen *et al.* 1980). This result was achieved after analysing tissue sections cut at right angles to each other, and serially. Consequently, only one tissue section of each lobe is needed for morphometrical analysis. The hilus area of the lobe, however, was excluded because of its somewhat differing histological appearance (stereologic structure). The hilus contains more or less unidirectional tubules studded with flattened epithelium not present elsewhere in the ventral prostate. Also, the proportion of interacinar tissue seemed to be higher in the hilus than in the parenchyma of the gland. The hilus area consisted of 5·4 % ±2·4 (S.D.) of the whole ventral prostate lobe as determined with the aid of the point-counting method from three normal rats.

(2) *Morphometrical analysis*

The tissue sections were examined with a Wild M 501 semiautomatic sampling microscope (Wild Heerbrugg Ltd, Heerbrugg, Switzerland), equipped with a projection head. The Weibel multipurpose graticule with 120 points and 60 test lines (Fig. 1 *a*) was inserted into the head. The systematic field sample technique was used. The computations were performed either at magnification × 43 (controls to day 5 after castration) or × 86 (7 to 30 days after castration). The use of different magnifications was based on the fact that in control animals, and in rats with minor degrees of prostatic atrophy, the tissue compartments could well be discerned at magnification × 43, whereas in animals with more extensive tissue atrophy, higher magnification was needed to notice the relevant structures. The use of different magnifications had no effect on the results.

Table 1. *Weight of the rats (at the end of the observation period)*

(Values are given as means ±S.D. Numbers in parentheses refer to the number of rats per interval.)

	0 days	12 hours	1 day	2 days	3 days	5 days	7 days	10 days	20 days	30 days
Castrated		299±27 (5)	323±18 (5)	311±18 (4)	303±27 (4)	308±34 (4)	335±18 (4)	281±5 (4)	341±19 (4)	340±41 (4)
Controls	319±24 (25)									

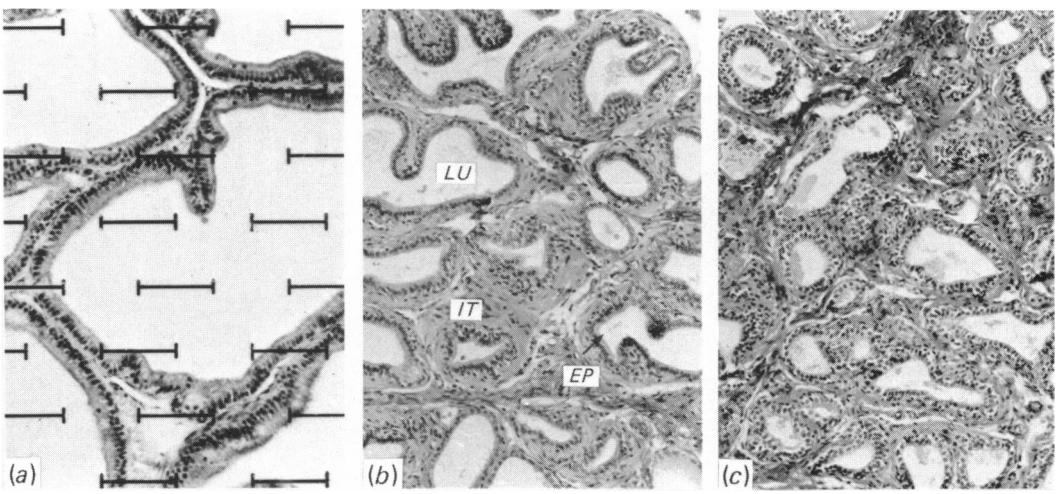

Fig. 1 (*a–c*). Light microscopic structure of the rat ventral prostate. (*a*) normal, showing a part of the graticule for stereological measurements; (*b*) 10 days; (*c*) 30 days after castration. *IT*, interacinar tissue; *EP*, glandular epithelium. *LU*, glandular lumen. Van Gieson's method for collagen fibres. × 86.

(*A*) *Volumetric fractions* (V_V) (mm^3/mm^3). The point-counting method, the principles of which were developed by Delesse, was used (cf. Bartsch & Rohr, 1977). The volumetric fraction (V_{Vi}) was gained by dividing the number of points on a tissue compartment (P_i) by the total number of points (P_T):

$$V_{Vi} = \frac{P_i}{P_T}. \tag{1}$$

The rat prostate tissue was divided into two major compartments: (i) acinar parenchyma (V_{VAP}), and (ii) interacinar tissue (V_{VIT}), which was the tissue outside the basal lamina of the epithelium (connective tissue, smooth muscle cells, nerves, vascular and lymphatic channels). The acinar parenchyma was further divided into (iii) glandular epithelium (V_{VEP}), and (iv) glandular lumen (V_{VLU}) (Fig. 1*b*). For each specimen the sample size was 600 points, which decreased the relative error below the 10% level (Romppanen *et al.* 1980). The 'Holmes effect' was corrected according to Weibel & Paumgartner (1978):

$$V_{Vi\ (\text{corrected})} = V_{V\ (\text{counted})} - (\text{or} +)\ \tfrac{1}{4} \times d \times S_{Vi}, \tag{2}$$

where d is the section thickness, and S_{Vi} the surface density of the overlapping

boundary, e.g. the surface density of the glandular epithelium. As reported earlier (Romppanen *et al.* 1980), the magnitude of this correction was 3 to 7 %.

(*B*) *Surface density of the glandular epithelium* (S_{VEP}) (mm^2/mm^3). The surface area of a given tissue structure per unit volume of the tissue (S_V) could be calculated from the number of intersections (I_i), formed by intersections of the cut surfaces of the structure at the test line system on a definite length (L_T) (Weibel, 1963; Underwood, 1970):

$$S_V = 2 \times \frac{I_i}{L_T}. \tag{3}$$

The determination of the (S_{VEP}) was performed by counting the intersections of the test lines at the luminal border of the glandular epithelium.

(*C*) *Length density of glandular tubules* (L_V) (mm/mm^3). The length of the prostatic glandular tubules per unit volume (L_V) could be calculated from the formula:

$$L_V = 2 \times Q_A, \tag{4}$$

where Q_A is the number of profiles of the cylinders per unit area at the section plane (Weibel, 1963; Underwood, 1970). Four test screen areas were counted according to the unbiased counting rule (Gundersen, 1977).

(*D*). *Parameters for the whole ventral prostate.* So far all parameters (*Prm* = V_V, S_V, L_V, see above) have been relative ones, the reference volume being 1 mm^3 of prostatic tissue. To describe the tissue alterations in a more satisfactory way, the values of *V*, *S*, and *L* were also calculated per total volume basis of both ventral lobes. According to DeKlerk & Coffey (1978), 1 mg of fresh rat ventral prostate tissue had a volume of approximately 1 mm^3. Consequently, the weight of the ventral lobe (Vol_{PR}; mg) could, in practice, be used as equivalent to volume (mm^3):

$$Prm \text{ (whole prostate)} = Prm \text{ (per 1 mm}^3\text{)} \times Vol_{PR}. \tag{5}$$

(*E*). *Stereologic calculations.* The following stereologic derivatives were calculated (cf. Romppanen *et al.* 1980):

(a) Mean height of the glandular epithelium (h) (mm):

$$h = \frac{V_{VEP}}{S_{VEP}}. \tag{6}$$

(b) Mean diameter of the glandular tubules (D_{AP}) (mm). This was determined in two different ways. First, using the mean intercept length as equivalent to the true diameter of the (cylindrical) glandular tubules (Underwood, 1970):

$$D_{AP1} = \bar{L}_{3LU} + 2h = 4 \times \frac{V_{VLU}}{S_{VEP}}, \tag{7}$$

where $\bar{L}_{3LU}$ = mean intercept length of cylinders made up by glandular lumen. Second, the previously calculated value of (V_{VLU}) and (L_V) could be utilized:

$$D_{3AP} = 2 \times \sqrt{\frac{V_{VLU}}{\pi \times L_V}} + 2 \times h. \tag{8}$$

(c) Mean free distance between the glandular tubules (λ_{AP}) (mm). The mean free distance between the glandular tubules was calculated from the formula (Underwood, 1970; Romppanen *et al.* 1980):

$$\lambda_{AP} = \lambda_{LU} - 2h = 4 \times \frac{1 - V_{VLU}}{S_{VEP}} - 2h \tag{9}$$

the (λ_{AP}) designated the 'thickness' of the interacinar tissue between the glandular tubules (Fig. 1). (λ_{AP}) was the mean distance between the glandular lumina (from inner epithelial surface to inner epithelial surface).

(d) Mean distance between the glandular centres (σ) (mm). According to Underwood (1970), and our previous report (Romppanen *et al.* 1980), the mean distance between the glandular centres (σ) could be calculated from the formula:

$$\sigma = \bar{L}_{3LU} + \lambda_{LU}. \quad (10)$$

For each point in Figures 2–7 at least 4 determinations were carried out. The significance of the difference between two means was assessed with Student's *t*-test.

RESULTS

Castration induced rapid changes in the light microscopical appearance of the ventral prostate (Fig. 1). The proportion of the interacinar tissue appeared to increase, while that of epithelium and lumen seemed to decrease (Fig. 1).

In Figure 2 the volumetric fractions of the various tissue compartments are shown. The proportion of the interacinar tissue (V_{VIT}) increased from 0·13 mm^3/mm^3 to 0·51 mm^3/mm^3 during the observation period (Fig. 2*a*). Correspondingly the proportion of acinar parenchyma (V_{VAP}) decreased from 0·87 mm^3/mm^3 to 0·49 mm^3/mm^3 (Fig. 2*b*). At 12 hours there was a transient increase in the amount of interacinar tissue (Fig. 2*a*), and a corresponding decrease in the acinar parenchyma (Fig. 2*b*). The response of the glandular epithelium to castration was rapid (Fig. 2*c*, see also Fig. 3*d*). The lowest value of the glandular epithelium (V_{VEP}) was already reached at day 2; it decreased from 0·42 mm^3/mm^3 to 0·26 mm^3/mm^3, whereas at day 30 the value was 0·29 mm^3/mm^3 (Fig. 2*c*). The proportion of glandular lumen (V_{VLU}) first increased from 0·44 mm^3/mm^3 to 0·59 mm^3/mm^3 at day 2, whereafter it decreased to 0·19 mm^3/mm^3 (Fig. 2*d*).

The influence of castration on the weight of the ventral prostate (Vol_{PR}) is given in Figure 3*a*. At day 3, two thirds, day 6, one third, and day 30, one tenth of the original weight (301 mg) was left. The total amounts (fractional weights) of different tissue compartments are given in Figures 3*b–e*. The amount of interacinar tissue first increased at 12 hours (from 40 mg to 60 mg), but from then on decreased to 15 mg (Fig. 3*b*). The difference at 12 hours was statistically significant ($P < 0·025$) when compared with the controls. The fractional weight of acinar parenchyma, (261 mg in normal rats) was reduced to two thirds at day $2\frac{1}{2}$, to one third at day $5\frac{1}{2}$, and to one tenth at day 18 (Fig. 3*c*). The reduction was statistically significant ($P < 0·01$) at day 2. Glandular epithelium, on the other hand, decreased to two thirds (80 mg) of the original value (126 mg) at about day 1, to one third at day 4, and to one tenth at day 20 (Fig. 3*d*). Decrease in the fractional weight of the epithelium was significant ($P < 0·01$) at 12 hours and highly significant ($P < 0·001$) at day 1. The amount of glandular lumen (normal 135 mg) first appeared to increase (the increment was not significant in Student's *t*-test), the peak was reached at day 1 (145 mg), and thereafter decreased to 6 mg at day 30 (Fig. 3*e*). At day 2 after castration, the fractional amount of lumen was equal to that of normal rats (Fig. 3*e*).

The surface density (S_{VEP}) increased from 11 mm^2/mm^3 to 17 mm^2/mm^3 during the observation period (Fig. 4*a*). The total epithelial surface (S_{EPPR}) (3375 mm^2 in controls), however, decreased to two thirds at day $4\frac{1}{2}$, to one third at day $8\frac{1}{2}$, and almost reached the one tenth level at day 30 (486 mm^2) (Fig. 4*b*). At 12 hours there

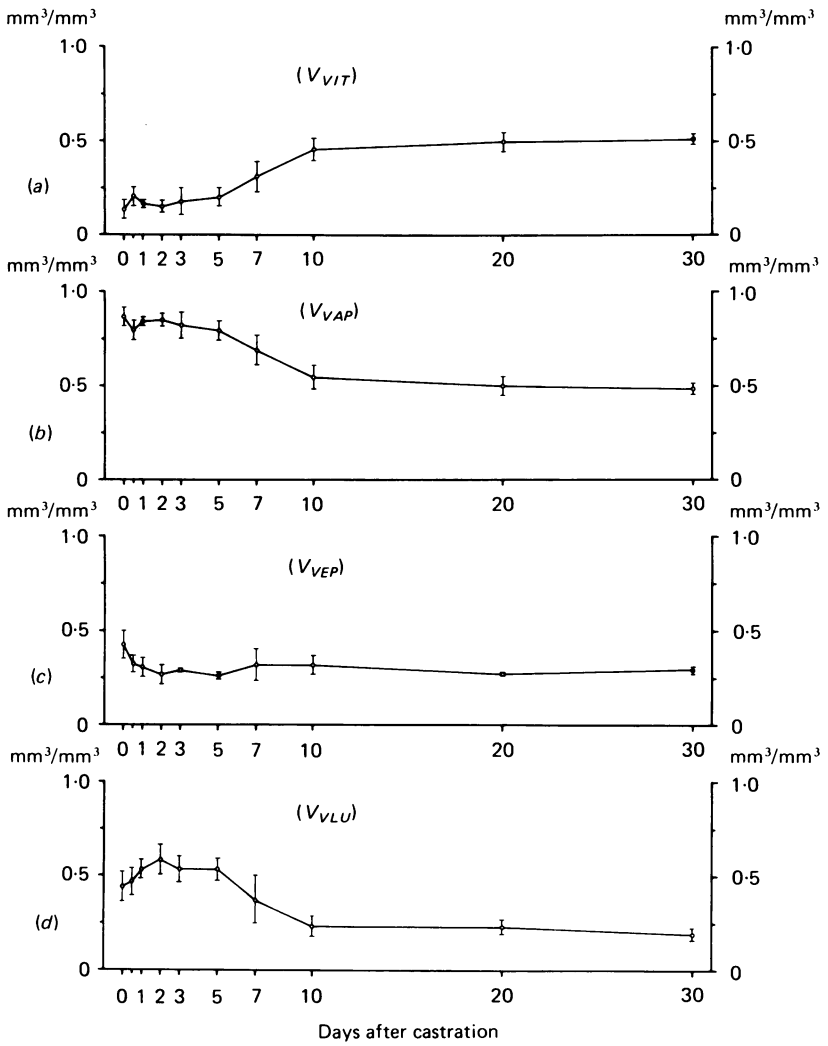

Fig. 2 (*a–d*). The effect of castration on the volumetric fractions (V_V) of different tissue compartments in the rat ventral prostate. (*a*) interacinar tissue (V_{VIT}); (*b*) acinar parenchyma (V_{VAP}); (*c*) glandular epithelium (V_{VEP}); (*d*) glandular lumen (V_{VLU}). *Ordinate*: mm³/mm³; *abscissa*: days after castration. The vertical bars designate the standard deviation (S.D.).

was a peculiar notch downwards in the curve, which was compensated at day 1 (Fig. 4*b*).

The length density (L_V) of the glandular tubules increased from 18 mm/mm³ to 112 mm/mm³ during the observation period (Fig. 5*a*). A rapid increase of values was noted between days 5 and 10. The total length (L_{PR}) of the glandular tubules decreased from 5371 mm to 3244 mm at day 30 (Fig. 5*b*).

The height of the glandular epithelium (*h*) was quickly lowered from 0·038 mm to 0·025 mm at day 1, whereafter the reduction was less drastic. The decrease in height was statistically significant already at 12 hours ($P < 0{\cdot}025$). At day 30 the value was 0·018 mm. This value was already reached at day 5 (Fig. 6).

The mean diameter of the glandular tubules (D_{AP}) decreased from 0·25 to 0·26 mm

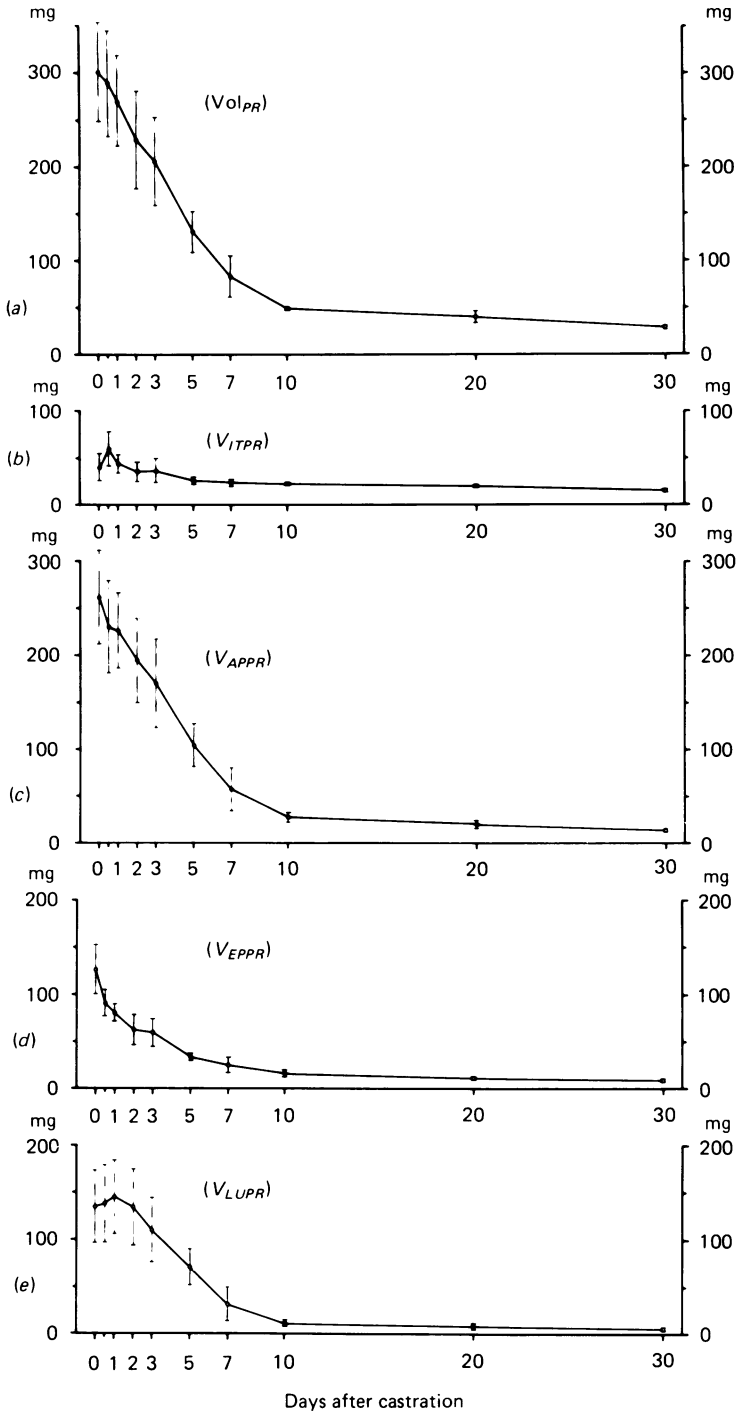

Fig. 3 (*a–e*). The effect of castration on the weight and total amounts of different tissue compartments in the rat ventral prostate. (*a*) weight of ventral prostate (Vol_{PR}); (*b*) interacinar tissue (V_{ITPR}); (*c*) acinar parenchyma (V_{APPR}); (*d*) glandular epithelium (V_{EPPR}); (*e*) glandular lumen (V_{LUPR}). *Ordinate*: mg; *abscissa*: days after castration. The vertical bars designate the S.D.

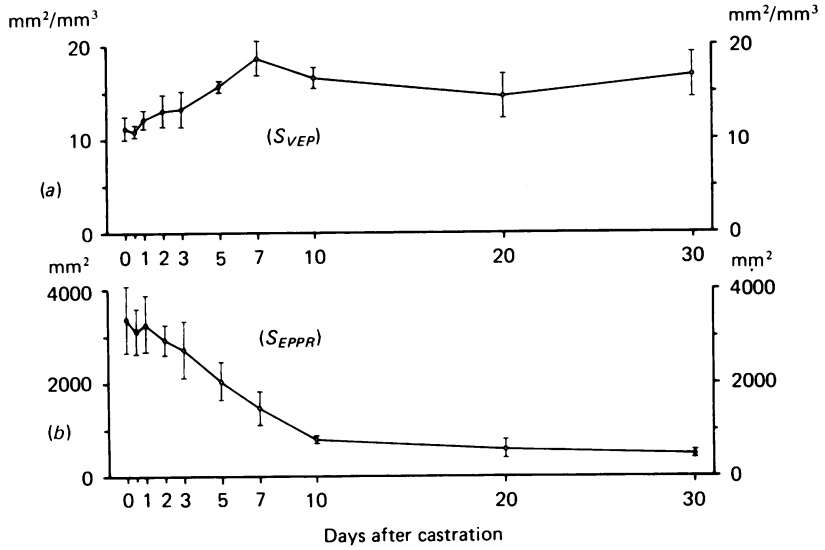

Fig. 4 (*a–b*). The effect of castration on (*a*) the surface density (S_{VEP}) of the glandular epithelium, and (*b*) total epithelial surface (S_{EPPR}) of the whole ventral prostate. *Ordinate*: (*a*) mm²/mm³; (*b*) mm²; *abscissa*: days after castration. The vertical bars designate the S.D.

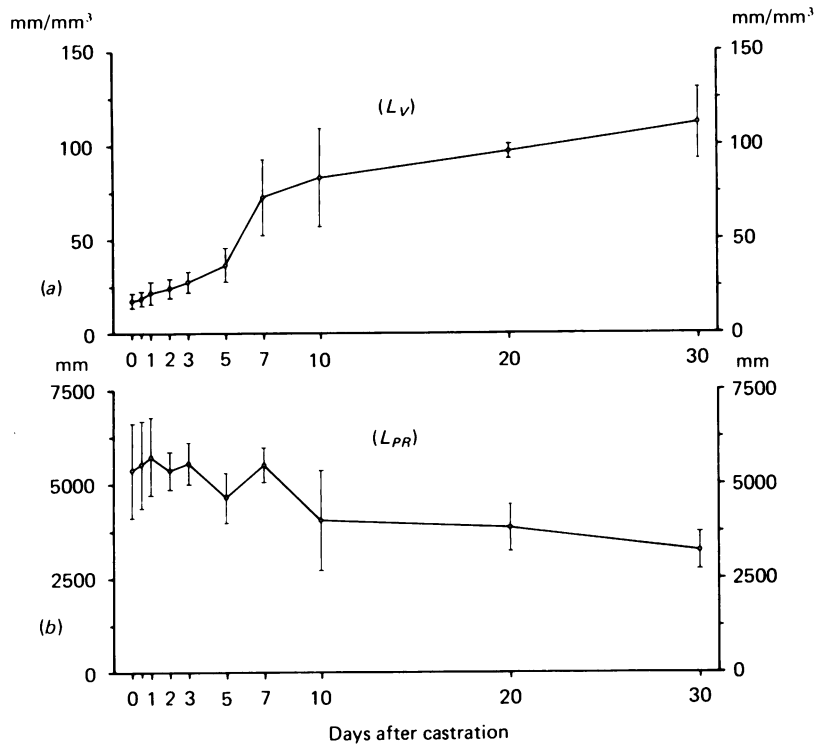

Fig. 5 (*a–b*). The effect of castration on (*a*) the length density (L_V) of the glandular tubules, and (*b*) total length of the glandular tubules (L_{PR}) of the whole ventral prostate. *Ordinate*: (*a*) mm/mm³; (*b*) mm; *abscissa*: days after castration. The vertical bars designate the S.D.

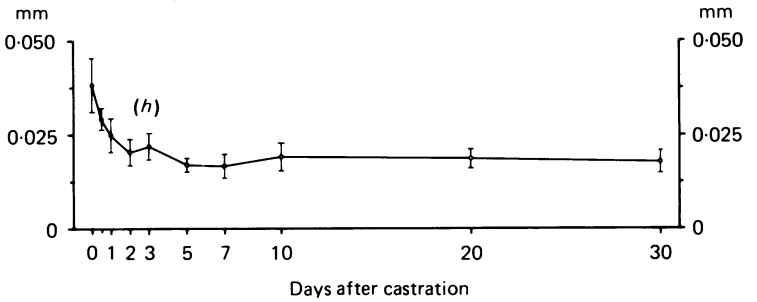

Fig. 6. Height of the glandular epithelium (*h*) after castration. *Ordinate*: mm; *abscissa*: days after castration. The vertical bars designate the S.D.

to two thirds of the original value at day 5, and to one third at day 30 (Figs. 7*a*, *b*). The mean free distance between the glandular tubules (λ_{AP}), the 'thickness' of the interacinar tissue, first (at 12 hours) increased from 0·125 mm to 0·135 mm (Fig. 7*c*), but from then on decreased to about 0·09 mm at day 3 to 5, rising again to a level of 0·18 to 0·16 mm at days 20 and 30 (Fig. 7*c*). The mean distance between the glandular centres (σ) decreased rapidly after castration (from 0·36 mm to 0·22 mm at day 7), while the distance slowly increased to 0·24 mm until day 30.

DISCUSSION

Stereology means the application of mathematical axioms (geometrical probabilities) to reconstitution and simultaneous quantitation of three dimensional structures from measurements on two dimensional cross sections, e.g. tissue sections. The method allows the quantitation of such parameters as the volume (V), surface (S), length (L), and number (N) of different tissue structures (Weibel, 1963; Underwood, 1970; Rohr, Oberholzer, Bartsch & Keller, 1976). The calculated quantitative data of a three dimensional tissue component i is expressed as volume density (V_{Vi}), surface density (S_{Vi}), length density (L_{Vi}), and numerical density (N_{Vi}) within unit volume of the reference space. This technique is by far superior to the traditional descriptive or qualitative methods used in histology, inasmuch as the method ensures the numerical expression and statistical treatment of the results and thus is very valuable for studies on tissue structure alterations.

There are, however, pre-requisites which have to be met before adequate use of a histoquantitative method is possible. First, the stereologic model of the tissue has to be outlined. Different tissue compartments in the sections, and their boundaries, as well as arrangement in the reference space and geometrical shape of the structures has to be determined. Second, the degree of orientation of the tissue structures must be defined. When planar or linear structures are randomly oriented (the surfaces of the structures have no favourite direction, nor orientation axis), as in this study, sections cut in one direction only can be used for stereologic morphometrical analysis. Third, the distribution of the tissue structures within the reference volume is a matter of importance, which also has to be settled. Also, the variation of parameters between different sections and microscopical fields must be determined. This knowledge gives an insight into the necessary sample size to keep the method within acceptable limits of error. As a rule, the standard error of the mean of a parameter should be less than 10%, when the values of a sample are compared with each other (Weibel, 1963; Bartsch & Rohr, 1977). Fourth, the

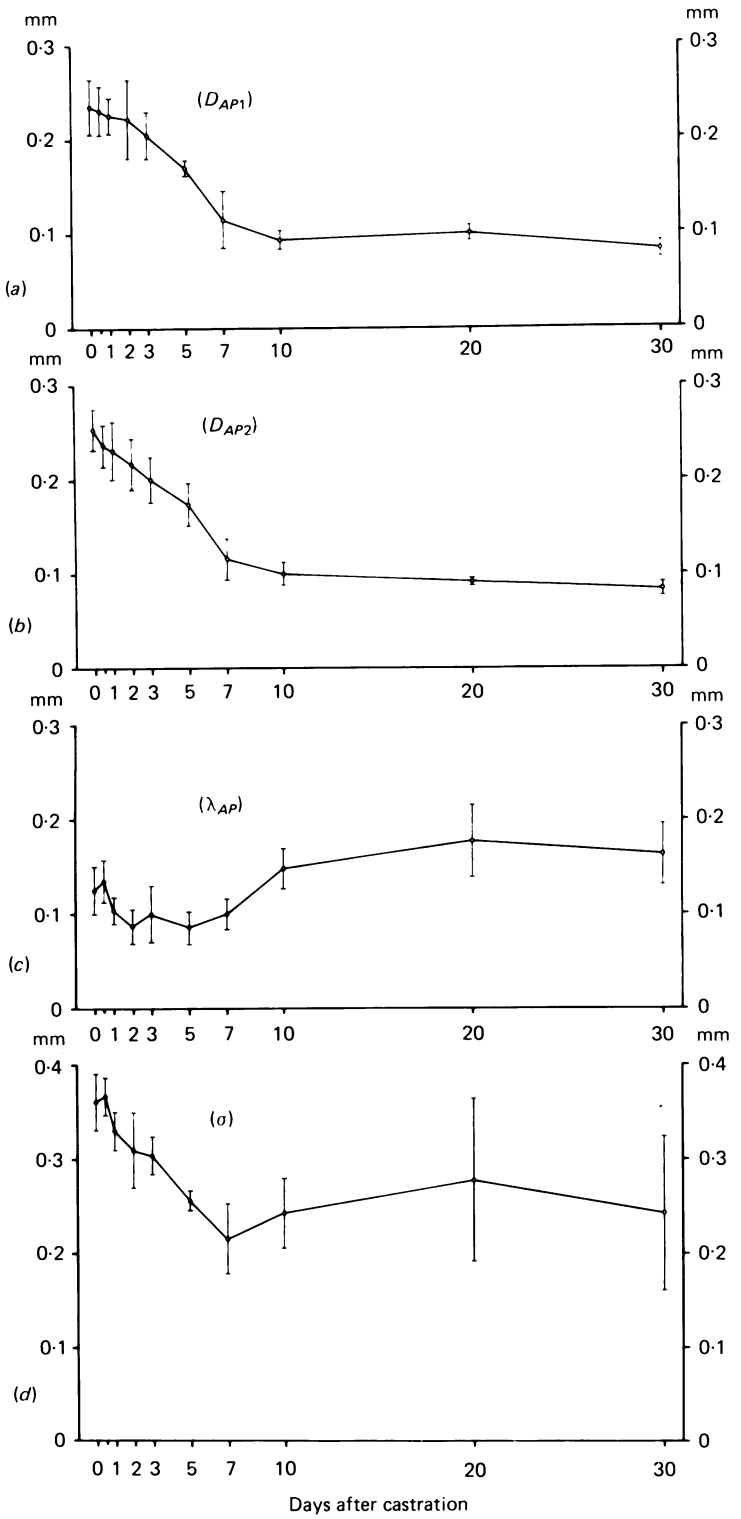

Fig. 7 (*a–d*). The effect of castration on the mean diameter (D_{AP}) of the glandular tubules. In (*a*) D_{AP1} is estimated from the mean intercept length, eq. 7, and (*b*) D_{AP2} from V_{VLU} and L_V, eq. 8. (*c*) presents the mean free distance of the glandular tubules (λ_{AP}), and (*d*) the mean distance between the glandular centres (σ). *Ordinate*: mm; *abscissa*: days after castration. Vertical bars designate the S.D.

effect of technical artifacts on the calculated values, due to fixation, embedding, tissue cutting and staining must be reduced to a minimum. This requires strict standardization of the histological procedures used.

Although all details mentioned above were taken into consideration in the planning and execution of the present study, there always remain sources of error which influence the results gained. One of them was the pre-supposition that the glandular structures are cylinders, although they often have foldings and saccular extensions. Another was the assumption that the specific gravity of the ventral prostate was equal to 1·0, although, according to DeKlerk & Coffey 1978), it was about 1·04 for freshly prepared tissue. The correct figure would actually be the one measured after fixation, dehydration, embedding, cutting and staining. However, since the measurement of the true specific gravity would have been difficult, the value 1·0 was considered proper. Therefore, it must be borne in mind that all the values obtained were more or less relative, even if the 'total amount' or fractional weight of a tissue compartment was in question. In all, however, the basic requirements for the use of a histoquantitative method were met in this study. For further discussion on methodology see Bartsch & Rohr (1977), DeKlerk & Coffey (1978) and Romppanen *et al.* (1980).

In previous investigations, castration-induced prostatic atrophy has been observed by aid of histoquantitative methods in some detail. Arvola (1961) observed (during a period of 270 days) alterations in the prostatic tissue utilizing a linear measurement method; the first intervals for quantitative studies were 10, 21 and 42 days. According to Arvola, the volumetric fraction of epithelium remained about constant at 10 %, that of lumen decreased from 70 % to 18 %, and the proportion of stroma increased from 20 to about 80 %. The 'weight indices' or fractional weights (total amounts of tissue compartments) were calculated in the same way, and with the same reservations, as in the present study. The weight index of the lumen dropped to 1–3 %, and that of epithelium to 5–13 % of the normal value. In line with the results of the present investigation, Arvola (1961) was able to show the decline in the weight index of stroma, which was about 37–47 % of the normal value 270 days after castration. DeKlerk & Coffey (1978) reported in their elegant study that, 17 days after castration, a 92 % decrease in the total epithelial cell number, and an 85 % decrease in the epithelial cell size could be observed while stromal cell number was reduced by only 39 %, and size by 23 %.

The present investigation throws more light on the process of tissue atrophy in the prostatic tissue, inasmuch as the tissue changes have been observed at close intervals after castration, and new histoquantitative parameters have been introduced. The process of prostatic atrophy has not been investigated earlier in such detail. It is notable that castration reduced the fractional weight of epithelium very rapidly (Fig. 2*d*), while the corresponding value for lumen decreased more slowly (Fig. 2*e*). The height of the epithelium was reduced to one half two days after castration (Fig. 6), which gives an indication of the speed of the process. The surface area (Fig. 4) declined more rapidly than the length of the tubules (Fig. 5). This is explicable, since the diameter of the glandular tubules decreased rapidly after day 2 (Figs. 7*a*, *b*), and the epithelium proved to be especially sensitive to androgen deprivation.

The reaction of the interacinar tissue to castration was also interesting (Figs. 2*a*, 3*b*). Its volumetric fraction increased during castration, while, on the other hand, its fractional weight decreased to one third. This observation corroborated

the results of Arvola (1961) and DeKlerk & Coffey (1978). However, 12 hours after castration, there was an initial elevation of the fractional weight of interacinar tissue by one third of the original value (Fig. 3*b*). The difference was significant when compared with ventral prostates of the controls ($P < 0{\cdot}025$). After the 12 hours interval, however, the decline of interacinar tissue was steady. It can be postulated that on account of withdrawal of androgenic hormones, injury of the cells or intercellular matrix was induced, and was followed by an inflammatory reaction with oedema in the interacinar tissue. As shown here and earlier, the epithelial cells react rapidly to lack of androgenic hormones (Harkin, 1957; Helminen & Ericsson, 1971; Brandes, 1974; Aumüller, 1979). However, it is also possible, although perhaps less probable, that the interacinar tissue, which is especially abundant in smooth muscle cells and fibroblasts (Flickinger, 1972), would immediately react to lack of androgenic hormones. At all events, this alternative must be remembered, since it has been shown that the stroma underlying the prostatic epithelium has at least supporting or permissive function (Franks *et al.* 1970; Cunha & Lung, 1979), if not inducing or directing, i.e. "directing or instructing the epithelium to pursue a pathway different from its normal developmental fate" (Cunha & Lung, 1979; Cunha, 1973). The studies of DeKlerk & Scott (1978), Kellokumpu-Lehtinen, Santti & Pelliniemi (1979), and Müntzing *et al.* (1979) also stress the significance of the stromal tissue in conjunction with the development, or growth, of the prostatic epithelium.

In conclusion, the present investigation allowed a stereologic morphometrical approach to tissue alterations which take place in the ventral prostate after castration. The prostatic epithelium was heavily and rapidly affected by the withdrawal of testosterone. At the same time the lumina of the glandular acini reacted more slowly. After an initial rise, the amount of interacinar tissue was reduced to one third, while the epithelium and acinar parenchyma were reduced to one tenth of the original value. The surface area of the prostatic epithelium decreased to 15% of the normal level. At the same time the length of the prostatic tubules was reduced by only 40%. The 'thickness' of the interacinar tissue was almost doubled during castration. This was probably due to the conspicuous diminution of the diameter of the prostatic tubules, since the reduction in the mean distance of glandular centres was less significant.

SUMMARY

The effects of castration on the rat ventral prostate was studied utilizing an improved histoquantitative technique. Both volumetric fractions of the tissue compartments and their fractional weights, or, 'total amounts', were calculated during an observation period of 30 days. In addition, the surface area, length and mean diameter of the glandular tubules were recorded. The changes in the mean free distance between the tubules ('thickness' of the interacinar tissue) and the mean distance between the glandular centres were also determined. It was observed that the prostatic epithelium was quickly reduced in thickness after castration, to one half at day 2. Decline of the fractional amount of the lumen was slower; it also reached below the 10% level at day 30. The amount of interacinar tissue first increased at 12 hours by one third, but from then on decreased to one third of the normal amount. The 'thickness' of the stroma almost doubled, which was probably due to the sum of the simultaneous marked decline in the diameter of the tubules to one third of the original and the less striking reduction to two thirds of the mean

distance between the glandular centres. The morphometrical method ensured the acquisition of a quantitative insight into the tissue processes involved in prostatic atrophy. Calculation of the fractional weights was regarded as especially invaluable, inasmuch as a growing body of evidence has been accumulated in favour of the crucial role of stromal-epithelial interactions in the differentiation, and growth, of the prostate.

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