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Invited Review

The female prostate and prostate-specific antigen. Immunohistochemical localization, implications of this prostate marker in women and reasons for using the term "prostate" in the human female

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Summary. Prostate-specific antigen (PSA) is currently the most frequently used marker for the identification of normal and pathologically altered prostatic tissue in the male and female. Immunohistochemically PSA is expressed in the highly specialized apically-superficial layer of female and male secretory cells of the prostate gland, as well as in uroepithelial cells at other sites of the urogenital tract of both sexes. Unique active moieties of cells of the female and the male prostate gland and in other parts of the urogenital tract are indicative of secretory and protective function of specialized prostatic and uroepithelial cells with strong immunological properties given by the presence of PSA. In clinical practice, PSA is a valuable marker for the diagnosis and monitoring of diseases of the male and the female prostate, especially carcinoma. In the female, similarly as in the male, the prostate (Skene's gland) is the principal source of PSA. The value of PSA in women increases in the pathological female prostate, e.g., carcinoma. Nevertheless, the total amount of PSA in the female is the sum of normal or pathological female prostate and non-prostatic female tissues production, e.g., of diseased female breast tissue. The expression of an antigen specific for the male prostate, i.e., PSA in female Skene's glands and ducts, and structural and functional parameters and diseases similar to that of the male prostate, have provided convincing evidence of the existence of a prostate in women and definitive preference of the term "prostate" over that of Skene's glands and ducts. The use of the term Skene's glands incorrectly implies that some other structure rather than prostate is involved, promoting the vestigial position of this female organ.

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Introduction

Reinier de Graaf (1641-1673), a Dutch physiologist and histologist, was the first to describe the female prostate and to assign it this term (de Graaf, 1672). One year before his death, de Graaf (1672) described in his work "De mulierum organis generationi inservientibus . . . ." exactly, and perfectly for his time, the structure of the female prostate as being formed by glands and ducts located around the female urethra. De Graaf was also the first who attempted to formulate the function of the female prostate on writing: "The function of the prostate (corpus glandulosum) is to generate a pituitoserous juice which makes women more libidinous with its pungency and saltiness and lubricates their sexual parts in agreeable fashion during coitus" (Jocelyn and Setchell, 1972). Although de Graaf's notion of homology of the female paraurethral glands and ducts as the female prostate with the male prostate was essentially but an intuitive idea, he is doubtless the discoverer of the female prostate and should be accepted and acknowledged as such.

Some 200 years after de Graaf, the American gynecologist, Alexander J.C. Skene (1838-1900), redescribed the female prostate as being comprised of two main paraurethral ducts that bear his name - Skene's glands - opening on both sides of the urethral orifice (Skene, 1880). Following Skene's description, the origin, and even the presence and function of these (para)urethral ducts and glands, became the subject of considerable debate. This contributed to a general

increasing lack of attention and importance to the female prostate, and the structures comprising it remained essentially anatomical curiosities until the studies of Huffman in the late 1940s and 1950s (Huffman, 1948, 1951). In spite of the elegant studies of Huffman (1948, 1951), including re-attention to Skene's glands as being the homologue of the male prostate in the female and of their clinical significance to date, the female prostate has been, in the authors' opinion, incorrectly termed by Skene's name. Observations substantiating the opinion that the female prostatic tissue should be referred to as female prostate, similarly as in the male, have been convincingly accumulating (Zaviačič et al., 1985a, 1997a,b; Zaviačič, 1987b; Zaviačič and Whipple, 1993; Sesterhenn et al., 1998; Zaviačič and Ablin, 1998a,b).

The issue of the female prostate has attracted the attention of such renown personalities of biology and medicine as Astruc (1737), Virchow (1853), as well as several others (as reviewed by Huffman [1948] and Stifter [1988]).

The time of the great pathologist Rudolf Virchow (1821-1902) was a particularly favorable period for the study of the female prostate. Professor Virchow was concerned with the controversy of the female prostate, which he acknowledged as a female genitourinary organ in its own right. He was the first to describe concrements "corpora amylacea", in the glands of the female prostate (Virchow, 1853), which up to that time had been known to be present only in the male prostate. In view of Professor Virchow's great professional authority, his observations prompted further inquiry into the controversy of the female prostate for a long period after his death.

The clinical interest in the issue of the female prostate was at the time of Virchow much less pronounced than that of morphologists and this situation persisted up to the early 1980s. Presently, we are witnessing an increasing clinical interest of urologists and gynecologists in the female prostate, especially in relation to the new knowledge on prostate-specific antigen (PSA) in the female and its potential implications for women. Although extraprostatic sources of PSA are being intensively investigated in the male and female (Diamandis and Yu, 1995; Diamandis, 1998), the female prostate, similarly as that of the male, is considered to be the main producer of this prostatic marker in the female (Zaviačič and Ablin, 1998a,b; Zaviačič et al., 1998a). The lesser heretofore, clinical interest in the female prostate may be accounted for by the fact that compared to the male, the female prostate is generally thought to be less affected by diseases, and moreover, these are mostly not as severe as in the male. And, with exception of recent consideration of the female urethral syndrome by Gittes and Nakamura (1996), no exact clinico-pathological data are available either on the diseases of the female prostate or on the actual incidence of these disorders in women.

The term female prostate was commonly used until the beginning of the 20th century. The designation was at that time substantiated especially by embryologic data demonstrating that the male prostate and Skene's glands are both derived from the same embryonal tissue, i.e., the urogenital sinus. Even to date, some textbooks provide these data as the only argument in favor of the homology between the male prostate and Skene's glands - the female prostate (Campbell, 1954; Egloff, 1972; Kurman, 1994). However, embryologic data alone supporting the homology of the two genitourinary structures have been considered insufficient for the unambiguous acceptance of the existence of the female prostate as a gland in its own right.

On the other hand, an opposite trend appeared from the beginning of our century which considered the female prostate, referred to as Skene's paraurethral ducts and glands to be an insignificant rudimentary vestigial organ without any importance in the life of women. The vestigial concept of the female prostate was predominantly based on gross macroscopic differences in the size of the prostatic glands in the two sexes. For some investigators the difference in size favoring the male prostate provided a comfortable perspective for the non-functionality of the female prostate or at least as being not as fully functional as its male counterpart. And yet, the human body presents many examples refuting this presumption. For example, the pituitary, notwithstanding its small size, is a central endocrine organ controlling the function of the other endocrine organs and through them that of the whole organism.

The vestigial concept of the female prostate has been supported by the fact that in the majority of women it fails to be a focus of clinical problems. Further, there is no exact answer to the question whether, and to what degree is, the female prostate an organ whose function is hormonally-dependent. This appears to be a strong argument since the male prostate provides a classical example of a hormonally, i.e., androgen-dependent organ.

Those interested in the history of the female prostate, spanning the range from the vestigial notion of Skene's gland to the current nonvestigial concept, which has been developing from the early 1980s, may find relevant information in our previous publications dealing with this issue, including the doctoral thesis of one of us (MZ [Zaviačič, 1985a, 1987b; Zaviačič et al., 1985a; Zaviačič and Whipple, 1993]). The work of Stifter (1988) provides a historically broad approach to the controversy of the female prostate and its role in the female ejaculatory phenomenon, as well as valuable information on the evaluation of the female ejaculation in different cultural settings, including that in ancient India and Japan.

Earlier studies originating in the first half of the 20th century also deserve to be mentioned, and these included the work of Evatt (1911), Johnson (1926), Korenchevsky (1937), Petrowa et al. (1939), Caldwell (1941), Folsom and O'Brien (1943, 1945), and Deter et al. (1946). These studies contributed to the gradual shaping of ideas concerning this small female organ, which later led

Huffman (1948, 1951) to reach conclusions on the orthology and pathology of the female prostate, which have been positively affecting the increasing interest in the study of this urogenital organ up to the present day.

The current intensive investigation of the female prostate, with its beginning dating back to the early 1980s, has yielded findings demonstrating this small organ of the female urogenital system as an organ with defined structure and function. Evermore morphological and clinical parameters have been detected which have proved to be corresponding or well comparable with those of the male prostate, and their number keeps increasing.

Our review deals with functional-morphological and some clinical aspects of the normal and pathological female prostate. The value of prostatic markers, particularly PSA, as well as of further parameters important in studying the structure and function of the female prostate are pointed out. The major part of this review is focused primarily on the last 20 years, i.e., the period starting with the early 1980s. This has been a period of intensive methodological advances and of increasing clinical interest in this female genitourinary organ. The intensive research and increased publications on the female prostate the last 20 years appears to have generally changed our views on this small female organ, as documented by differences in opinion of the same investigators presented in papers published within a relatively short time span. For example, Dr. Sesterhenn, as a coauthor of Wernert's paper on the female prostate (Wernert et al., 1992), wrote: "They (glands of the female prostate) remain immature throughout life from the fetal period up to the advanced age . . . . No indications can be found for a proper biological function." Six years later, the same investigator (Sesterhenn et al., 1998) wrote: "The female prostate is not a myth and is not equivalent to Skene's glands . . . . It (the female prostate) does explain detectable serum PSA levels in females." We are confident that this change in opinion may have been reflected in part by the substantial investigations of the female prostate by one of us (MZ) over the last 15 years (Zaviačič et al., 1985a,

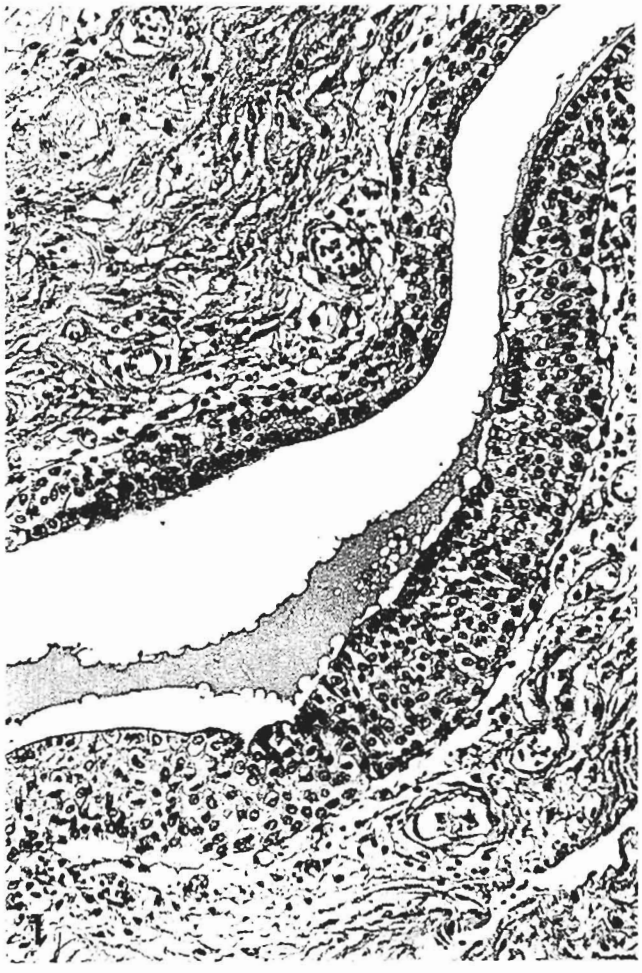

Fig. 1. One great duct of the female prostate lined by pseudostratified columnar epithelium. In the lumen residua of the prostatic fluid. 58 year old female, Haemotoxylin and eosin (HE), x 180

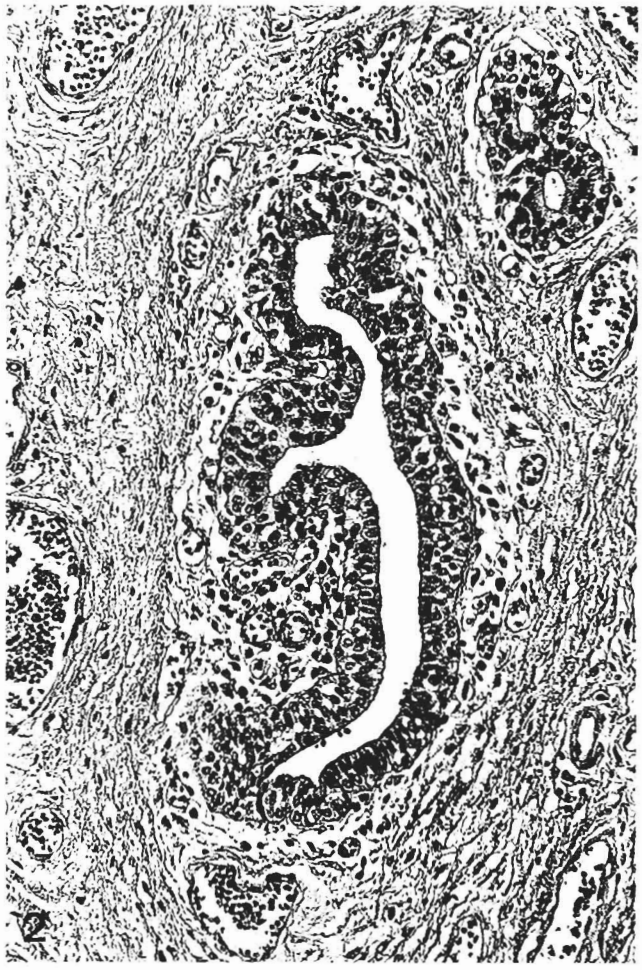

Fig. 2. One medium duct and two glands of the female prostate. 58 year old female HE, x 180.

1994; Zaviačič, 1987b and references therein), as well as our recent communications (Zaviačič and Ablin, 1998a,b).

PSA: Immunohistochemical localization in tissues of the female and male prostate, serological parameters and implications of this prostate marker in the female and in the male

At present PSA is generally accepted as the most useful biological marker of male prostate carcinoma (PCa) and has become the mainstay for screening, in monitoring response to therapy and in predicting outcome of this carcinoma (Ablin, 1996, 1997, and references therein).

Immunohistochemical evidence of PSA plays a crucial role in the identification of normal and pathologically altered prostate tissue in the male (Nadji et al., 1981; Epstein and Eggleston, 1984; Purnell et al., 1984; Stein et al., 1984; Svanholm, 1986; Jöbsis, 1990; Keillor and Aterman, 1993). Equal importance of the immunohistochemical demonstration of PSA is to be assigned also to the identification of normal (Pollen and Dreilinger, 1984; Tepper et al., 1984; Wernert et al., 1992; Zaviačič et al., 1994) and pathological (Svanholm et al., 1987; Wernert, 1991; Zaviačič et al., 1993; Sloboda et al., 1998 and references therein) prostatic tissue in the female.

Before presenting selected findings of the immunohistochemical evidence of PSA in the female prostate, it is useful for the purpose of orientation to illustrate the basic structure of the female prostate and the appearance therein of the prostatic ducts (Figs. 1-3) and prostatic glands (Figs. 4-5).

Our findings obtained at autopsy and on detailed examinations of urethras from over 150 women are in conformity with the configuration of the female prostate as described by Huffman (1948), including the existence of not only two ducts as described by Skene (1880), but numerous ducts, as well as the prevalence of prostatic tissue in the anterior urethra (Zaviačič, 1987b). Paraurethral glands (glands of the female prostate) are

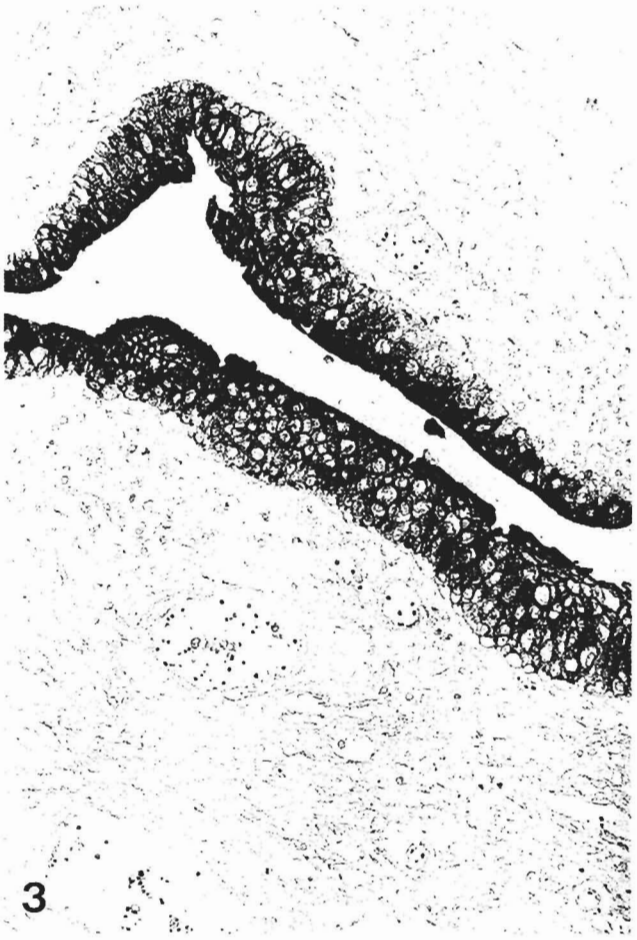

Fig. 3. Great duct of the female prostate with expression of cytokeratins (an epithelial marker) in superficial and apical parts and membranes of pseudostratified columnar epithelial cells lining the lumen of prostatic duct. Cytokeratin clone AE1/AE3 monoclonal antibody, 60 year old female, x 180

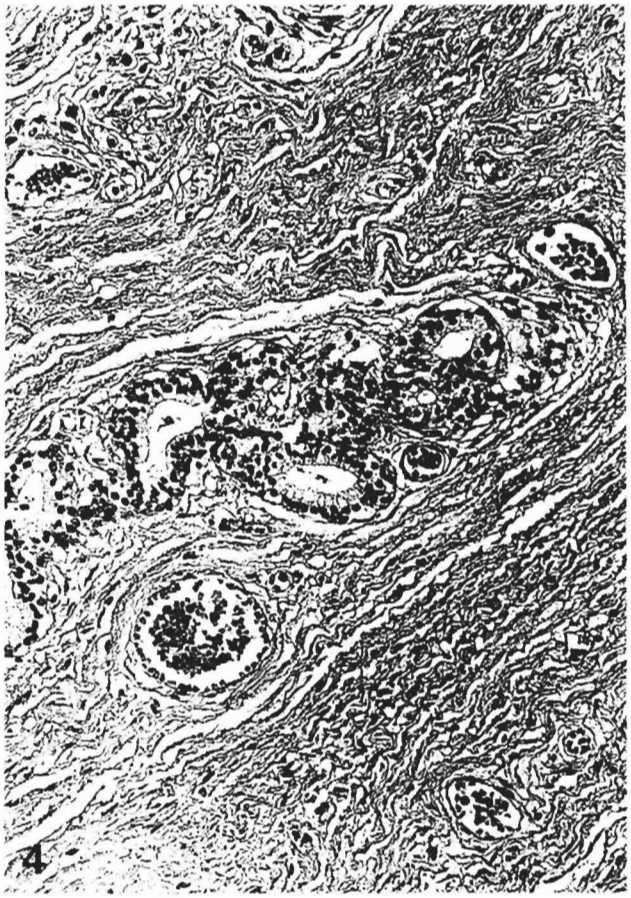

Fig. 4. Group of glands of the female prostate. 39 year old female, HE, x 180

lined by columnar, cuboidal to moderately tall cylindrical cells (Fig. 5). Light microscopy permits differentiation of secretory and basal cells in female prostate glands according to the shape of the cells, their nuclei and localization. The existence of these cells in the female prostate, initially refuted by Wernert et al. (1992), has subsequently been definitively established by electron microscopic studies of Sloboda et al. (1998) and Zaviačič et al. (1998b). The ducts of the female prostate (paraurethral ducts) are lined by pseudostratified columnar epithelium (Figs. 1-3). Near the orifices of the ducts in the lumen of female urethra, the lining becomes the same type as that of the urethra (Zaviačič et al., 1983).

Immunohistochemical examination of PSA using polyclonal antibodies by peroxidase anti-peroxidase (PAP) technique (Figs. 6, 7) and by the method of biotin-streptavidin-alkaline phosphatase (Figs. 8, 9) yielded expression of the examined marker in the highly specialized apically superficial layer of female secretory (luminal) cells of the female prostatic glands and membranes of secretory and basal cells and membranes of cells of pseudostratified columnar epithelium of ducts (Figs. 6-9). These findings (Zaviačič et al., 1994 and references therein, Zaviačič 1997) are in agreement with prostatic expression of PSA reported by others. Findings of the expression of PSA in prostatic secretory cells at the light microscopic level are concordant with immunoelectron microscopic localization of PSA in human male prostate by the protein A-Gold Complex (Sinha et al., 1987).

In keeping with the findings of Papotti et al. (1989) and other authors as reported by Diamandis and Yu (1995), we have standardly obtained results of high quality on using rabbit polyclonal antibodies (Figs. 6-10). The results with monoclonal mouse antibodies showed PSA positivity of varying intensity. In some instances no reaction was recorded in prostates of either sex. Examination of this prostate marker in male and female extraprostatic tissues showed invariably great

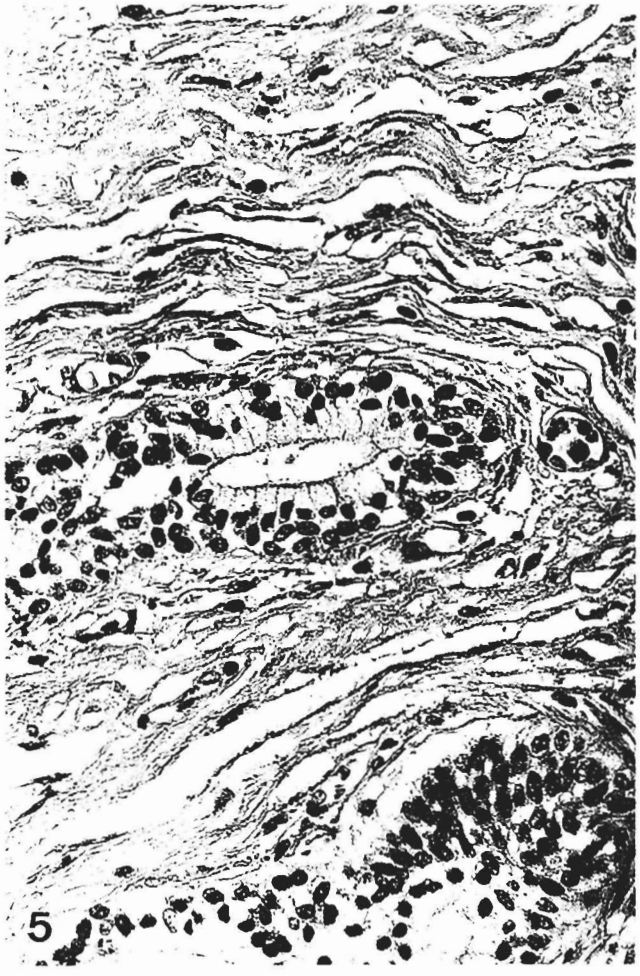

Fig. 5. Gland of the female prostate lined by columnar to moderately tall cylindrical secretory cells. Basal (reserve) cells have nuclei of different appearance, compare to secretory cells. 39 year old female, HE, x 360

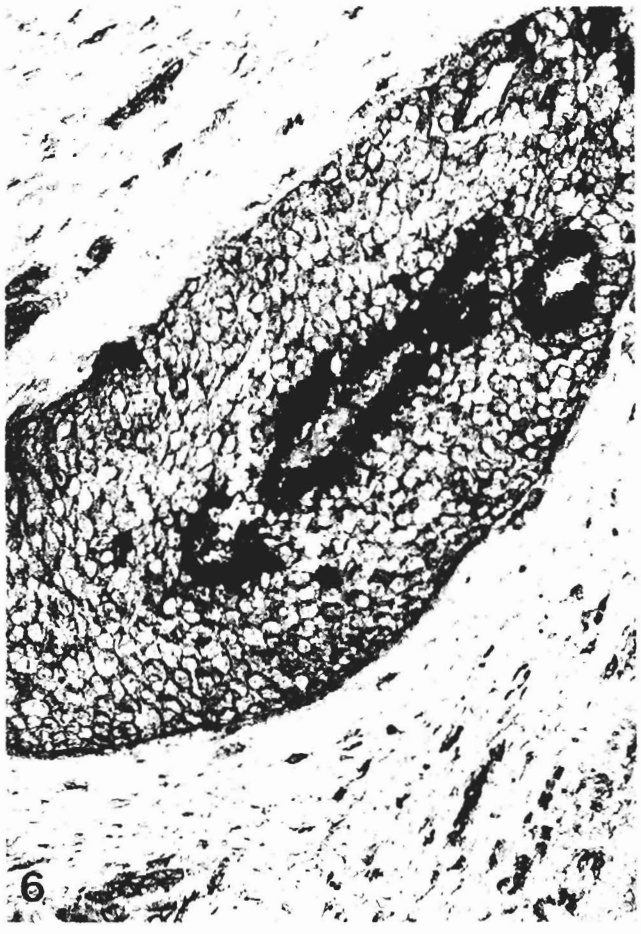

Fig. 6. Marked expression of prostate-specific antigen (PSA) in the apical part of cytoplasm of intraductal gland cells and in the superficial and apical part of cells lining the lumen of prostatic duct. Expression in membranes of pseudostratified columnar epithelium in the ductal lining. Peroxidase-antiperoxidase (PAP) method, 41 year old female, x 180

differences (Zaviačič et al., 1998a). In tissues of the male and female prostate, the two types of antibodies used yielded comparable results when necroptic prostatic tissue was studied after a longer period following death, as if autolysis would to some extent eliminate the differences between polyclonal (Fig. 10) and monoclonal antibodies (Fig. 11). We tended to examine male and female necroptic tissue within the shortest possible period after death, mostly 24 hours, since the length of duration of autolysis affected the immunohistochemical results unfavorably, even on using polyclonal antibodies for localization of PSA (Fig. 10).

In addition to secretory cells, PSA is expressed in membranes and on the surface of the epithelium of the luminal border of the ducts of the female and the male prostate. This unique layer of cells of the urogenital system is distinctly formed and richly supplied with glucosamine glucans, glycoproteins and enzymic proteins. In addition to numerous enzymes (Zaviačič, 1984a,b, 1985b) and the presence of human protein 1 (urinary protein 1 [Zaviačič et al., 1997a]), it has marked, and for the male and female prostate, distinct immunological properties given by the presence of antigen specific for the prostate.

Findings of immunohistochemical studies concerning PSA (Pollen and Dreilinger, 1984; Tepper et al., 1984; Wernert et al., 1992; Zaviačič et al., 1993, 1994; Zaviačič, 1997; Sloboda et al., 1998 and references therein) have broadened and enhanced the biological value of PSA, since this prostatic marker has been found relevant not only in studies of the male, but equally so, of the female prostate.

Clinically in males the reference range is about 1-2 ng/ml and values above 3-4 ng/ml are indicative of prostate cancer, benign prostatic hyperplasia or prostatitis (Borchert et al., 1997). A short update on the female prostate (Zaviačič and Ablin, 1998a,b) strongly suggests the possibility that in the female, similarly as in the male, the prostate (Skene's gland) is the principal

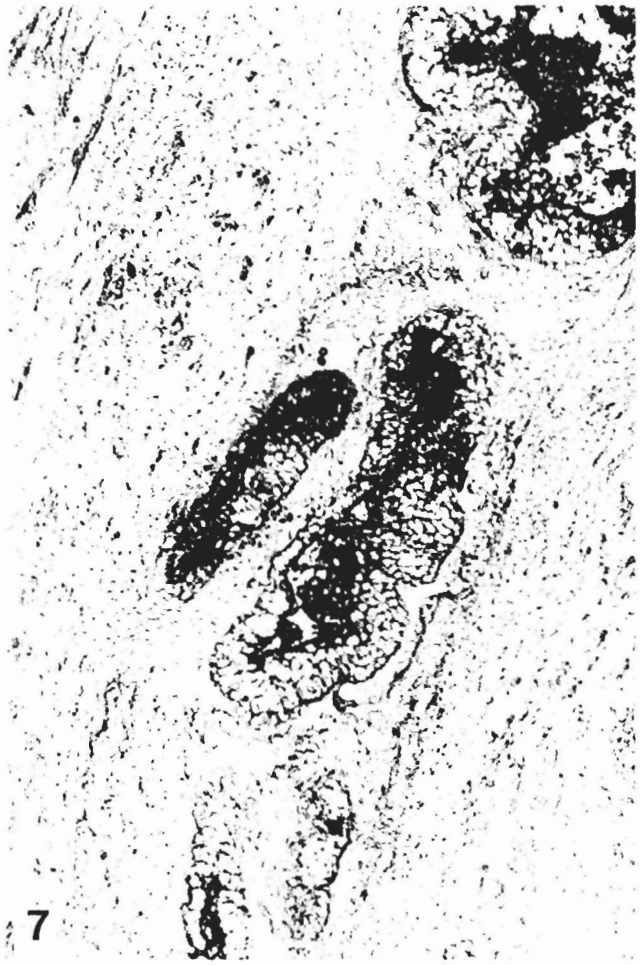

Fig. 7. Marked expression of PSA in luminal cells of the duct, in prostatic glandular cells and the fluid in the duct. 71 year old female, PAP technique, x 180

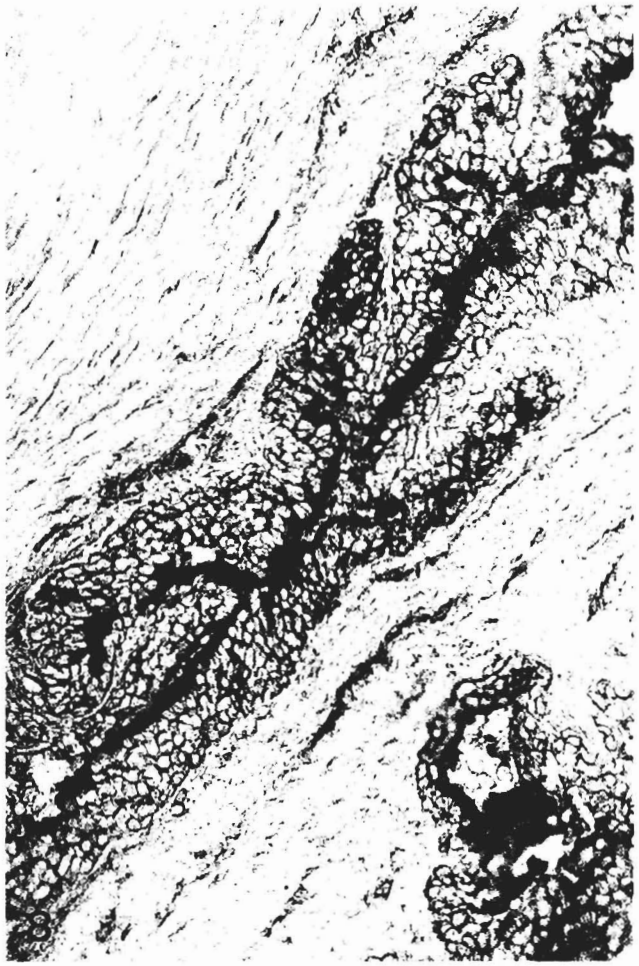

Fig. 8. Marked expression of PSA in the luminal part and membranes of pseudostratified columnar epithelial cells forming a prostatic duct. The expression continues to the apical cytoplasm of luminally localized cells. Biotin-streptavidin alkaline phosphatase (BSAP) method. 41 year old female, x 180

source of PSA in female serum and/or urine.

In addition to forensic medical implications in alleged cases of rape in the presence of the supposedly male specific markers PSA (p30 [Sensabaugh, 1978]) and prostate-specific acid phosphatase in the normal female ejaculatory fluid and vaginal secretions (Longo, 1982; Zaviačič et al., 1987a,b, 1988; Zaviačič and Ablin, 1998a), the participation of the female prostate in PSA production and its concentration in urine has been supported by the observations of Cabello (1997), who found significant differences in urinary PSA samples taken from the same women before and after orgasm. Evacuation of the female prostate induced by orgasmic contractions of the muscles surrounding the female urethra may account for the increased PSA values in urine after orgasm, as the content of the prostate with prostatic components, including PSA, is released into the urethra, and thus into urine.

A healthy female with a normal prostate is characterized by a broad range of serum PSA values from practically unappreciable amounts to the highest reported ones of 0.9 ng/ml (Borchert et al., 1997). This value is very close to the normal reference range in the male. Serological and/or urinary parameters of PSA in females are not surprising since they are well in line with the nonvestigial concept of the female prostate (Zaviačič et al., 1985a; Zaviačič, 1987b; Zaviačič and Whipple, 1993; Zaviačič and Ablin, 1998a,b), whose structure and function have been well established and its pathology broadly studied. These female parameters are very similar to those of the male prostate.

Increased serum PSA values may result from pathological changes of the female prostate itself, e.g., carcinoma of the prostate in the female, may induce a rise of up to 5.9 ng/ml (Dodson et al., 1994). The increase may represent a summation of values derived from PSA production of the normal female prostate (Skene's gland) according to Zaviačič and Ablin (1998a,b) and of possible nonprostatic tissue PSA origin, e.g., benign and malignant disease of the female breast (Diamandis et al., 1994; Yu et al., 1994, 1996; Borchert et al., 1997). In the female patient with breast fibroadenoma, serum PSA values are very high compared to female breast cancer, and may amount up to 55.1 ng/ml (Borchert et al., 1997), while the normal female and the normal male breast tissue according to our immuno-

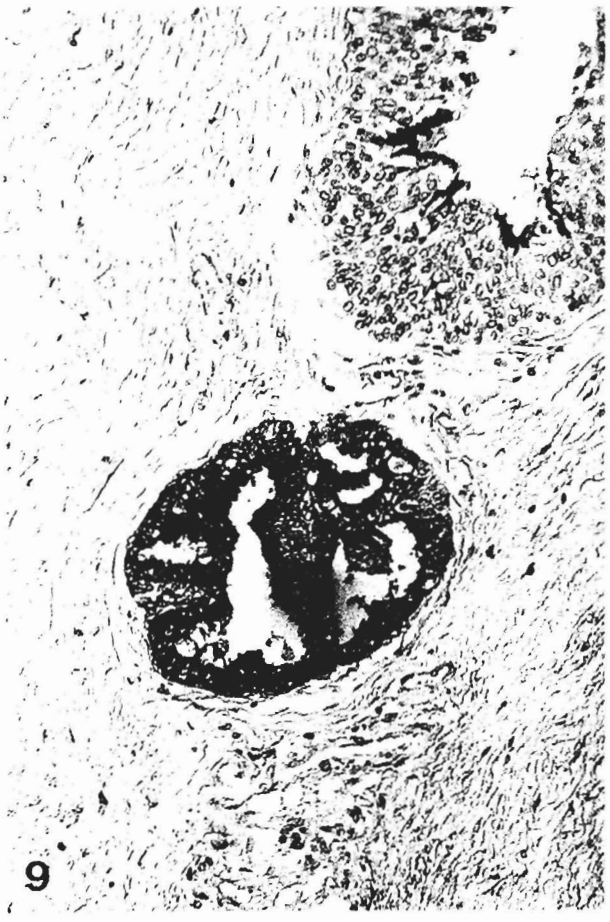

Fig. 9. Marked expression of PSA in apical part and surface of secretory (luminal) cells in the prostatic gland. 27 year old female, BSAP technique, x 180

Fig. 10. Low expression of PSA in glands of the female prostate after 72 hours of autolysis. 68 year old female, PAP technique, x 90

histochemical examinations produce no PSA (Zaviačič et al., 1998a).

One should be aware of the fact that every serum and/or urine PSA determination in the female inevitably involves a production by the normal or pathological female prostate (Skene's gland). It is very possible that novel, more sensitive serological methods recently introduced into clinical practice, e.g., Immulite-r immunochemiluminiscent third-generation assay (Diagnostic Products Corp., Los Angeles, CA) or other ultrasensitive tests, will enhance our knowledge on further parameters characterizing female PSA.

Reasons for rejection of the term Skene´s paraurethral ducts and glands for designation of the prostate in the human female

In the early decades of our century the term female prostate was used. Subsequently, the use of the term female prostate appeared only in sexologically oriented literature (Sevely and Bennett, 1978; Addiego et al., 1981; Belzer, 1981; Perry and Whipple, 1981; Bohlen, 1982; Ladas et al., 1982; Mallon, 1983; Belzer et al., 1984; Bullough et al., 1984; Heath, 1984; Zaviačič, 1987b), despite the fact that some sexologists raised arguments against the use of the term (Alzate and Hoch, 1986, 1988; Alzate, 1990). In the veterinary literature, the term female prostate was commonly used in describing prostatic tissue in females of different animal species (Shehata, 1972, 1975, 1980). Papers published in sexological of sexologically oriented journals contributed considerably to the use of the term female prostate at the time when other medical periodicals and texts maintained the official designation of "Skene's paraurethral ducts and glands."

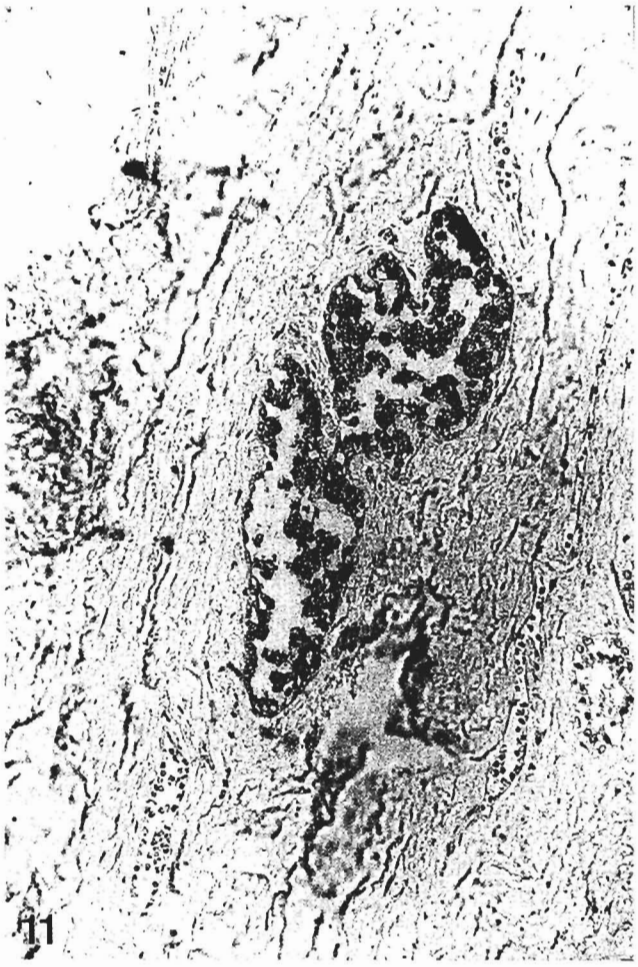

Fig. 11. Low expression of PSA in glands of the female prostate after 72 hours of autolysis. 68 year old female, mouse monoclonal antibodies, PAP technique, x 180

In the 1980s, and particularly in the second half of the decade, papers concerned with the female prostate, or female prostatic tissue as some of them referred to it, appeared also in journals with other than sexological orientation (Longo, 1982; Pollen and Dreilinger, 1984; Tepper et al., 1984; Zaviačič, 1984a,b, 1985a,b, 1986a,b, 1987a; Zaviačič et al., 1983, 1985a,b, 1987a,b, 1988, 1989). From the point of view of the past 15 years, Professor Raymond J. Wegmann, Editor-in-Chief of Molecular and Cellular Biology, deserves particular mention. As early as 1984 Professor Wegmann published, without any argument, the pioneering studies of one of us (MZ) on the enzymatic characteristics of the female prostate with the term "adult human female prostate" appearing in the title of the paper. Nonetheless, in the majority of subsequent papers submitted to other journals, it was still necessary to explain and defend this term over and over again in correspondence with the editors.

Nowadays the use of the term Skene's paraurethral ducts and glands for the female prostate fails to reflect the results published from the beginning of the 1980s to the present day in the field of research concerned with the female prostate. In his conclusions on the female prostate, Skene mistakenly focused his attention only on two paraurethral ducts, which fails to be in keeping with the actual situation as has repeatedly been pointed out by other investigators (Huffman, 1948, 1951; Zaviačič et al., 1983, 1985a; Zaviačič, 1987b; Wernert et al., 1992; Zaviačič and Whipple, 1993). Although Skene was concerned with the female prostate 200 years after de Graaf (Skene, 1880), it could hardly be maintained that he had elucidated the structure and function of this female gland so well, that it deserves to be designated by his name. Should we, however, insist on using eponyms, then the female prostate appears rightly to be termed after de Graaf, who discovered it in 1672. The return of de Graaf's term female prostate 300 years after he had introduced it has an explicitly rational and causal basis.

Particularly important contributions to the controversy over usage of the term "female prostate" were provided by: (1) the results of Mallon (1983), Pollen and Dreilinger (1984), Tepper et al. (1984), Zaviačič et al. (1994), Zaviačič (1995, 1997), who demonstrated expression of the heretofore thought of

male-specific antigen PSA in structures of Skene's paraurethral glands and ducts and (2) the commentary by Ablin (1989), who re-directed ". . . attention to the biological fact that women have a prostate gland" and that its presence explains the occurrence of PSA in female serum. This provided evidence and directed attention to the species, and not gender specificity of PSA between the male prostate gland and Skene's gland. Equally important are the results of histochemical studies investigating the enzymic characteristics of the female prostate (Zaviačič, 1984a,b), which was unknown until the 1980s. The enzymatic characteristics of the male and female prostate were found to be similar (Zaviačič, 1985b), including the immunohistochemical (Pollen and Dreilinger, 1984) and histochemical demonstration of prostatic and lysosomal acid phosphatase (Zaviačič, 1984b).

Expression of PSA in Skene's glands and ducts; the characteristic "prostatic" and lysosomal acid phosphatase in female Skene's glands; evidence of exocrine function and cellular capability for neuroendocrine function (Zaviačič et al., 1997b and references therein); the increasing number of papers reporting on diseases of the female prostate, as well as the implications of the exocrine function of the female prostate for gynecologic urology, forensic medicine, sexology, and chronobiology (Zaviačič et al., 1984, 1985a; Zaviačič, 1987b; Zaviačič and Whipple, 1993 and references therein) provided convincing evidence that it is actually prostatic tissue in the female and thus preference of the term female prostate over the term Skene's glands and ducts is fully justified (Zaviačič et al., 1985a; Zaviačič, 1987b). We cannot use the term "prostate" for the tissue in the male and a different term (i.e., Skene's glands and ducts) for the same tissue in the female. The use of the term Skene's glands and ducts wrongly implies that some other structure rather than prostate is involved, promoting the vestigial position of this female organ. Recognition of the female prostate is tantamount to providing women with appropriate medical treatment of an organ that is subject to the same diseases of their male counterpart. Furthermore, if the female prostate exhibits similar immunopermissiveness of the male prostate (Ablin and Gonder, 1985), it may also serve as a nidus for various infectious agents (Ablin, 1991) and proliferation of aberrant and retrogenic cellular alterations within the prostate.

In the light of the foregoing, we submit the request that the term female prostate be strictly used in the same meaning as this gland is designated and understood in the male. Due to the impact of the new situation shaped by acceptance of the new data on this female genitourinary organ, we advocate the renaissance of the term female prostate and its inclusions in the *Nomina Anatomica*. Currently the term *prostata feminina* is not used either by the Paris (1955) or by the New York (1960) and further anatomical nomenclatures. In the 1983 and 1989 *Nomina Anatomica* together with *Nomina Histologica and Ebryologica* the female prostate is found under the term "paraurethral ducts and glands" and the Skene's eponym is omitted. Nevertheless in clinical medical terminology, Skene's name for the designation of the female prostate is henceforth employed (Zaviačič, 1999).

The situation is probably the same as with the term *mamma masculina* and glandula mammaria *mamma feminina* (both are in the *Nomina Anatomica*) in spite of differences in the size of these structures in the female and the male, which in some cases are certainly greater than between the male and female prostate. Moreover, the male breast consists only of scattered ducts lined by epithelial and myoepithelial cells, embedded in fibrofatty connective tissue. Lactiferous sinuses are absent and there is no lobule formation (Ahmed, 1992). These structural insufficiencies of the male breast compared to the female breast and the exceptionally rare pathology of this male gland, restricted practically to the problem of gynecomastia and carcinoma, which moreover affects the male breast at a considerably later age than in females (Ahmed, 1992), have not been considered serious enough to exclude the term *mamma masculina* from the *Nomina Anatomica*. Even the greatest skeptic has to admit that the number of corresponding parameters in the male and female prostate exceeds by far those that are comparable between the male and female breast. And yet, the term female prostate has not been included in the *Nomina Anatomica*, while the terms male breast (*mamma masculina*) and female breast (*mamma feminina*) appear in the *Nomina Anatomica*.

On summarizing the data and knowledge accumulated so far on the female prostate, the idea of the prostate in the female as an insignificant, nonfunctional, vestigial Skene's gland (Skene's paraurethral glands and ducts in the female) is totally unsubstantiated.

The last more than 15 years of intensive investigations of the structure and ultrastructure (Zaviačič et al, 1998b), of the function and pathology of the female prostate and the wealth of information yielded by these studies have provided convincing evidence on this small organ as a functioning prostate of the female which deserves to be eventually included under the term "female prostate" in the *Nomina Anatomica*. In the light of extensive information presented in this review and elsewhere, the female prostate should receive a firm and equal position with other female genitourinary organs and particularly with the male prostate. This approach should be accepted not only by urologists, gynecologists and pathologists, but by all members of the biomedical community. For nobody, not even lay persons, should it be a "mystery female organ" any more.

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