Volume 2

Advances in Urology

Lytton • Catalona
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Advances in Urology

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Preface

The second volume of *Advances in Urology* continues with the original concept of bringing to the practicing urologist an overview of the significant areas of progress in the specialty. The articles in this volume deal with five topics: Diagnosis of Prostatic Cancer, Pediatric Urology, Retroperitoneal Lymph Node Dissection for Testis Cancer and Its Complications, Lower Urinary Tract Reconstruction in Children, and Sexually Transmitted Diseases with a special note on Acquired Immune Deficiency Disease. The contributors have all either been responsible for or have contributed to the innovations that they describe.

The first chapter is a clearly written and scholarly account of the role of prostatic specific antigen as a tumor marker in prostatic cancer. This sensitive immunological test, for a special protein produced by prostatic epithelium, is an important recent advance in cancer diagnosis and management. Its value and limitations need to be clearly understood, so Dr. Brendler's contribution is both useful and timely. This is followed by an excellent review of the current opinions on transrectal needle aspiration biopsy of the prostate by Drs. Bromberg and Graham from Northwestern University Medical School in Chicago. This is a valuable technique for use in the urologists's office, and it will probably be some time before it is replaced by the use of the new ultrasound-directed biopsies with a spring-loaded gun.

Chapters 3, 4, and 5 deal with the therapy for nonseminomatous germ cell tumors of the testis and with the management of some of the complications. Dr. Lange and his colleagues, Drs. Lightner and Fraley, have reviewed the many controversial issues regarding retroperitoneal lymph node dissection vs. surveillance in patients with Stage I disease. Drs. Oates and Lipshultz provide a very informative account, and discuss their experience with, the problems of infertility and testicular dysfunction in patients who have undergone systemic chemotherapy or radiation therapy for a variety of malignancies including testicular cancer. Drs. Bennett and Ohl have developed the use of electroejaculation to treat patients who become infertile following retroperitoneal lymph node dissection because of an inability to achieve satisfactory ejaculation. They describe their experiences with this modality, its indications, and its pitfalls.

The next chapter is by Dr. Berger and is an excellent summary of the current management of sexually transmitted diseases. He pays special attention to the biological aspects of transmission of HIV infection and details the precautions recommended to protect healthy workers from acquiring AIDS.

Chapter 7 reviews the current status of an important pediatric problem. Dr. Duckett has used his ingenuity and technical skills to bring about a major change in our management of the surgical correction of hypospadias. Successful one-stage procedures are now the rule rather than the excep-

tion. He and Dr. Keating give an excellent account, together with appropriate illustrations, of the state-of-the-art for the repair of these congenital urethral anomalies.

The advent of noninvasive imaging techniques, like ultrasonography, has led to the detection of many asymptomatic lesions. This has created a particular problem with urological abnormalities in the fetus. The ability to perform intrauterine surgery makes it of paramount importance to understand the significance of these findings. Dr. Lowell King places in perspective the interesting work that has been done on the evaluation of urological abnormalities in the fetus, and discusses the indications and timing of surgical management.

Chapters 8 and 10 deal with some of the novel methods now in use for the reconstruction of the lower urinary tract in children. Dr. Kropp has devised a successful new procedure for creating continence in children with neuropathic bladders secondary to myelodysplasia. Dr. Snyder reviews the numerous types of bowel segments used for reconstructive procedures and describes the experience in Philadelphia with the Mitrofanoff method of using a catheterizable segment of appendix or ureter as a continent stoma.

Chapter 11, by Dr. Ehrlich and his colleagues, Drs. Macfarlane and Koyle, is an excellent account of the present-day management of all stages of Wilms' tumor. Much of the information is derived from the outstanding work of the national Wilms' tumor study group of which Dr. Ehrlich is a member.

Bernard Lytton, M.B., F.R.C.S.

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Prostate-Specific Antigen: Significance in Evaluation of Men With Prostate Cancer

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Prostate-specific antigen (PSA) is a newly discovered glycoprotein that is produced exclusively by the epithelial cells of the prostate. Since its discovery in 1979, there has been considerable enthusiasm over its use as a tumor marker in prostate cancer. The purpose of this chapter will be to review the significance and role of PSA in the evaluation of men with prostatic carcinoma.

Characterization

PSA was first reported in 1979 by Wang and associates.[1] They discovered that rabbit antiserum raised against a crude extract of normal human prostatic tissue identified a prostate-specific antigen that was distinct from prostatic acid phosphatase (PAP). This antigen was detected in normal, malignant, and hyperplastic prostatic tissue but in no other human tissues. This new prostate antigen was subsequently purified to homogeneity from prostatic tissue and showed a single protein band on analytical polyacrylamide gel electrophoresis and isoelectric focusing. The purification procedure was subsequently improved[2] to yield 1 to 2 mg of purified PSA per 100 gm of benign prostatic hyperplasia (BPH) tissue. Subsequently, seminal plasma became the preferred material for isolation of PSA for three reasons: (1) the concentration of PSA is higher in seminal plasma (mean, 700 μg/mL) compared with BPH tissue (mean, 95 μg/gm); (2) seminal plasma contains fewer contaminating proteins such as hemoglobin; and (3) seminal plasma is more readily available than BPH tissue.

PSA is a glycoprotein that contains about 10% carbohydrate by weight; the molecular weight is between 33,000 and 34,000. It consists of a single polypeptide chain containing 240 amino acid residues. The isoelectric point is 6.9.[3] The concentration of PSA is similar in normal, hyperplastic, and malignant human prostatic tissue (approximately 11.0 μg/gm of tissue).[4]

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Characteristics of PSA compared with PAP are shown in Table 1. PSA and PAP are immunologically distinct; PSA does not react with anti-PAP serum, nor does PAP react with anti-PSA serum.[5]

Papsidero and associates[6] studied the localization of PSA in the prostate gland as well as in other tissues with immunoperoxidase staining. PSA is located exclusively within the cytoplasm of the epithelial cells of prostatic ducts. It is not found in the epithelia of other genitourinary tissues including the periurethral glands, seminal vesicles, vas deferentia, and transitional cell epithelium of the urinary bladder and prostatic urethra. PSA has not been detected in any other normal or nonprostatic malignant tissues including testis, kidney, intestine, stomach, salivary gland, colon, pancreas, liver, and breast.[7]

The primary structure and amino acid sequence of PSA has recently been determined.[8] PSA belongs to the family of serine proteases, a group of proteolytic enzymes of diverging specificity as collagenase, elastase, and the highly specific enzymes of the complement and coagulation systems. The serine proteases are characterized by the active site amino acid residues histidine, aspartic acid, and serine. PSA is structurally similar to pancreatic kallikrein. Although the function of PSA remains unclear, it has been shown to be involved in the liquefaction of seminal coagulum by proteolysis of its predominant protein component—a high molecular weight seminal vesicle protein or seminogelin.[9] The cDNA encoding PSA has recently been cloned.[10]

TABLE 1.
Characteristics of Prostatic Acid Phosphatase and Prostate-Specific Antigen*

	PSA	PAP
Molecular weight	33,000–34,000	100,000
Subunit	Single peptide	Dimer
Isoelectric point	6.9	4.2–5.5
Carbohydrate content (%)	10	7
Sedimentation coefficient	3.1 S	5.7 S
Electrophoresis mobility	β	α-β
Lectin-binding activity	+	+
Ammonium sulfate precipitation (% saturation)	45–50	50–70
Cell localization	Epithelial cells	Epithelial cells
Secretory nature	Yes	Yes

*From Kuriyama M, Loor R, Wang M, et al: Prostatic acid phosphatase and prostate-specific antigen in prostate cancer. *Int Adv Surg Oncol* 1982; 5:29–49. Used by permission.

Goldfarb and associates[11] have studied the age-related changes in tissue levels of both PSA and PAP by immunoperoxidase staining. Both PSA and PAP levels are high at birth, decrease by age 6 months, reappear by age 10 years, and subsequently increase until puberty. The levels of PSA and PAP appear to follow changes in serum testosterone levels, suggesting a hormonal dependence for both enzymes.

Section Summary

1. PSA is a glycoprotein that is produced exclusively by prostatic epithelial cells and is located exclusively within the cytoplasm. It has not been found in any other genitourinary tissues.
2. PSA is immunologically distinct from PAP.
3. PSA is a serine protease. Its function in the prostate is unknown, but it may have a role in liquefaction of seminal coagulum.
4. Serum levels of PSA, like PAP, fluctuate with changes in serum testosterone levels, suggesting a hormonal dependence.

Assay Methods

PSA is measured by radioimmunoassay (RIA) techniques. There are two methods currently available, both of which are marketed commercially as kits. The first is a classical polyclonal RIA for PSA (P-PSA) marketed by Yang Laboratories (Pros-Check PSA, Yang Laboratories, Inc, Bellevue, Wash). The second is a monoclonal immunoradiometric assay for PSA (M-PSA) produced by Hybritech, Inc (Tandem-R PSA, Hybritech, Inc, San Diego, Calif). The latter assay is the only one approved by the Food and Drug Administration for the evaluation of patients with prostatic cancer. Each technique is described briefly below.

In the P-PSA radioimmunoassay for PSA, a serum sample of 0.2 mL is incubated at room temperature for 18 hours with rabbit polyclonal antibodies directed against PSA. A second incubation at room temperature for 30 minutes with goat anti-rabbit antibodies precipitates the primary antibodies-PSA complex.

The M-PSA radioimmunoassay is a solid-phase two-site immunoradiometric assay. A serum sample of 0.05 mL is incubated at room temperature for 2 hours simultaneously with a plastic bead coated with a monoclonal antibody for a unique site of the PSA molecule and with an ^{125}I-labeled antibody directed against a different site of the PSA molecule. After the solid-phase-PSA–radiolabeled antibody sandwich is formed, the bead is washed to remove unbound labeled antibody. The radioactivity bound to the bead is measured in a scintillation counter.

Chan and associates[12] have recently evaluated the performances of both the P-PSA and M-MSA assays on patients with normal and abnormal prostate conditions including both BPH and prostatic carcinoma. Both the P-PSA and M-PSA immunoassays perform comparably well both analyti-

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