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PROSTATIC CARCINOMA
BIOLOGY AND DIAGNOSIS

edited by
E.S.E. Hafez and E. Spring-Mills

MARTINUS NIJHOFF

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FOREWORD

In the last decade substantial progress has been made in the understanding of prostatic physiopathology by the application of modern techniques and instrumentation in microanatomy, immunology, neurophysiology, pathology, genetics, endocrinology, biochemistry, biophysics and surgery. An attempt is made in this volume to coordinate anatomical, physiological, biochemical, endocrinological, pharmacological and immunological aspects of human prostatic carcinoma. It is hoped that this volume will serve as a stimulus to basic scientists and clinicians to intensify their research for better diagnostic techniques. Thanks are due to the contributors who prepared their chapters meticulously. Thanks also are due to Ms. Lori Rust for her editorial skills, and to Mr. Jeffrey Smith of Martinus Nijhoff for his fine cooperation during the production of this volume.

E.S.E. Hafez
Detroit, Michigan

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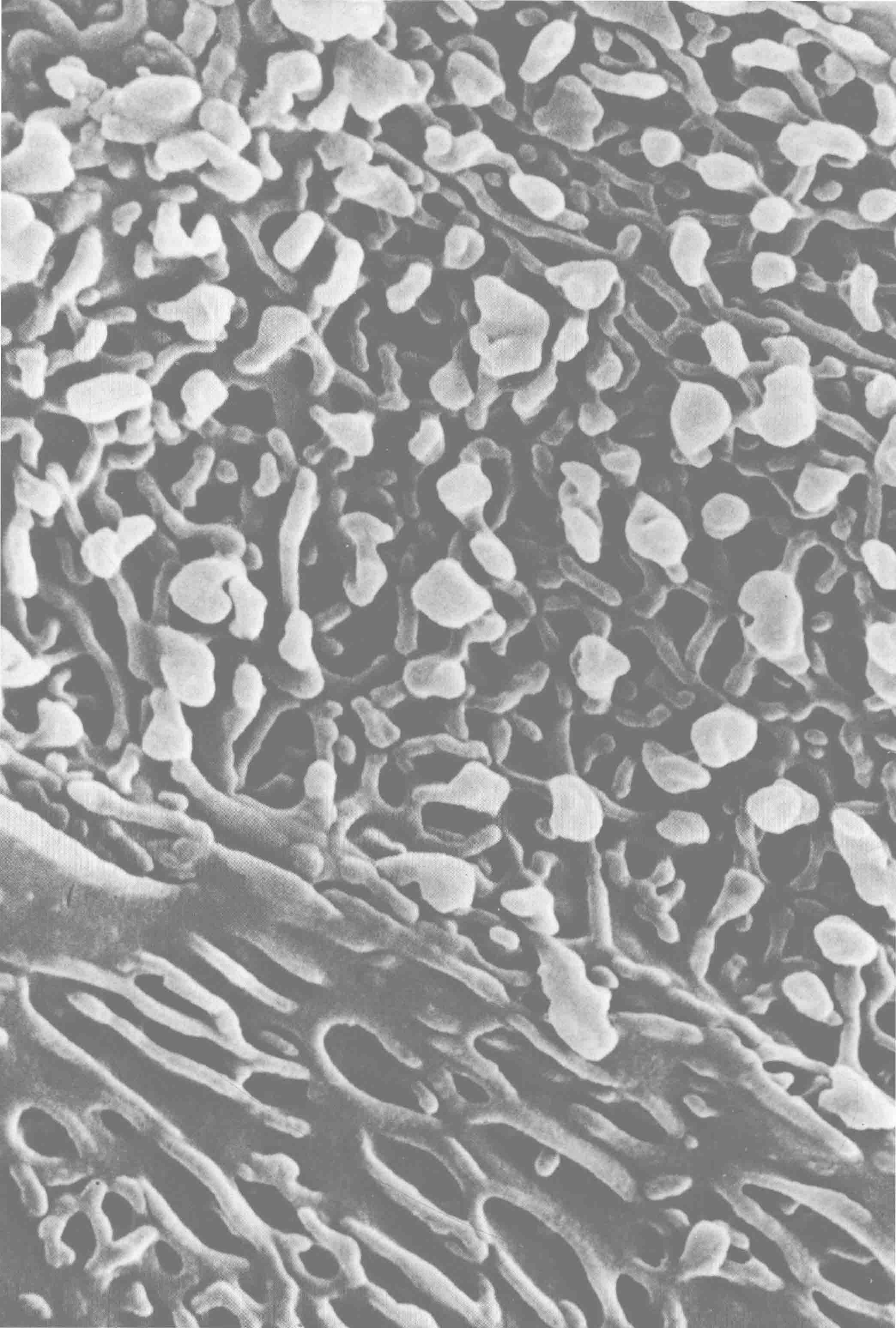

I. BIOLOGICAL ASPECTS

1. FUNCTIONAL ANATOMY OF THE PROSTATE

E. Spring-Mills and A. Krall

I. EMBRYOLOGY

The prostate gland develops from solid, endodermal outgrowths of urogenital sinus epithelium during the 12th week of gestation. The sinus is formed by the division of the cloaca into ventral (urogenital sinus) and dorsal (rectal) regions by the growth of the urorectal fold from the lateral walls. As the urorectal septum develops, the mesonephric or Wolffian ducts reach the cloaca caudal to the bladder. They aid in delineating the newly formed urogenital sinus and eventually give rise to the ductus deferens, seminal vesicles and ejaculatory ducts. The Müllerian ducts arise independently, lateral to the mesonephric ducts. During the 8th week of development, they grow caudally and rotate medially to contact the urogenital sinus in the midline at the swelling on the posterior urethral wall, the Müllerian tubercle. In the presence of the Müllerian inhibiting factor, these ducts quickly atrophy except for the fused distal remnant known as the prostatic utricle, a small blind-ended tubule (Patten 1968).

The classic study by Lowsley (1912) describes five groups of prostatic epithelial buds according to their relation to the prostatic utricle and ejaculatory ducts (Figure 1). The middle group of cords arises on the posterior wall of the sinus, superior to the utricle and limited by the ejaculatory ducts. Two lateral outgrowths develop from the lateral walls of the sinus. The posterior buds branch caudally to the prostatic utricle while the anterior cords arise from the anterior wall of the sinus. Although this anterior lobe is present in the fetus, it rapidly regresses in the neonate. In the adult, the distinction between the embryological lobes is masked.

As the cords grow, they induce the proliferation and differentiation of the surrounding mesenchyme into smooth muscle cells and collagen secreting fibroblasts. These cells form the stroma which ensheaths the branching glands and ejaculatory ducts as they pass from the junction of the vas deferens and seminal vesicles to the urethra.

The epithelium of a cord varies greatly in appearance. After canalization, it is composed of 2 cell layers with the principal cells cuboidal to low columnar. During the fifth month of gestation, tubules originating from the posterior wall of the urethra near the verumontanum as well as the prostatic utricle sometimes undergo squamous metaplasia. Regression of the metaplasia occurs through the first week postpartum. A PAS-positive lumenal secretion may persist a month or more after birth before subsiding; however, this secretion has not been observed in tubules with squamous metaplasia (Zondek and Zondek 1975, Brody and Goldman 1940).

During childhood, there is little further develop-

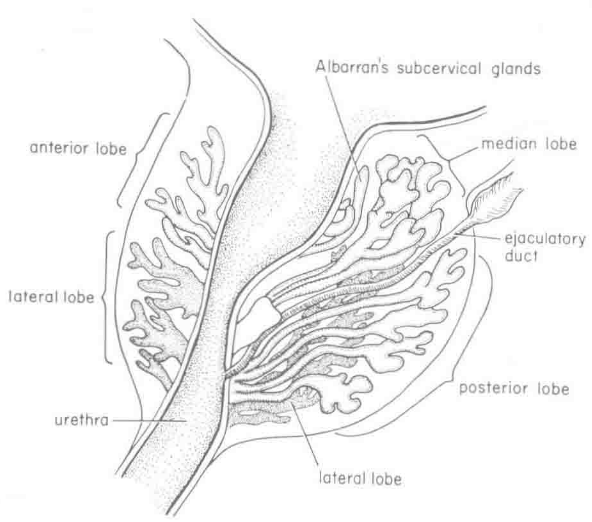

Figure 1. Line drawing illustrating the embryologic origins of the human prostate from the primitive urethra.

ment of the prostate. Some acinar proliferation occurs but the epithelium generally is cuboidal and quiescent. Few ducts from the anterior lobe remain; however, the lateral lobes extend anteriorly to encircle the urethra. At puberty, there is a relatively rapid increase in the size of the prostate. There is an expansion of the acini, an increase in lumenal diameter, and the appearance of tall columnar epithlium. Secretion resumes and continues throughout the life of a healthy individual (Swyer 1944).

II. GROSS ANATOMY

The prostate is situated at the neck of the bladder in the inferior portion of the pelvic cavity and surrounds the first segment of the urethra (Figure 2). It is triangular with the apex directed downward, contacting the urogenital diaphragm. The superiorly located base is continuous with the inferior aspect and neck of the bladder, but slightly separated from it by short, lateral and posterior grooves. Two convex lateral surfaces meet the levator ani fascia and join to form a rounded anterior edge. The edge passes posteriorly to the pubic symphysis. The posterior surface of the prostate is flattened and contacts inferiorly the urogenital diaphragm and the inferior rectum. It is this region which is palpated during a rectal examination. Great variation in the size of the prostate has

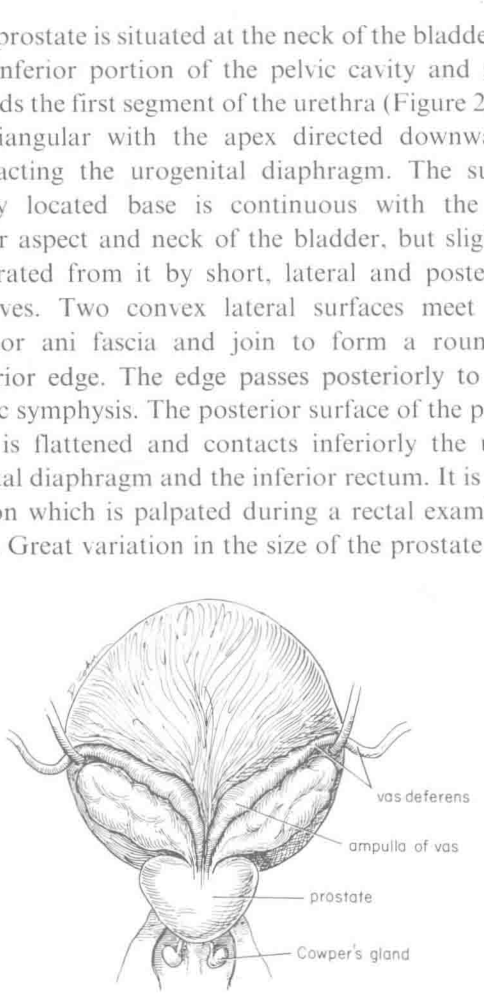

Figure 2. Line drawing illustrating the gross anatomical relationships of the bladder, ampulla of the vas deferens, seminal vesicles (unlabelled), prostate and Cowper's glands. Posterior view. From Spring-Mills E, Hafez ESE: Male accessory organs, In: Human reproduction, Hafez ESE, Evans TN, New York: Harper and Row, 1979.

been observed, but in the adult, it generally has a vertical length of 3 cm, frontal diameter of 4 cm, anteroposterior diameter of 2 cm, and a weight of approximately 20 gms. (Harrison 1972).

The 2 ejaculatory ducts penetrate the posterior surface at the upper border, anteroinferiorly traverse the glandular elements, and open into the urethra laterally to the verumontanum on the posterior wall. These orifices, in conjunction with that of the prostatic utricle, have been used as landmarks in delineating the lobes of the fetal and adult prostates. Although there is a consensus that the prostatic cords arise from 5 distinct regions of the urogenital sinus in the embryo, controversy still surrounds the lobation pattern of the adult gland. This stems from the use of different techniques to examine the gland (histology or step-sections versus gross dissection) and from the dogma established by Lowsley (1912) that benign hypertrophy and carcinoma arise in separate and distinct regions of the prostate. The two most commonly encountered schemas are the three butterfly-shaped pairs of lobes described by Tissell and Salander (1975) and the central and peripheral zones originally described by Huggins and Webster (1948) and later modified by others (Franks 1954, McNeal 1972).

A dense, fascial sheath encircles the entire prostate. The puboprostatic ligaments blend with this sheath anteriorly and laterally to anchor the gland to both the body of the pubis and the fascia of the levator ani muscles. Posteriorly, the prostatic fascia fuses with that of the ampulla of the ductus deferens and seminal vesicles to form the rectovesical septum which separates these structures from the rectum. (Harrison 1972)

Embedded within the fascial sheath are the vessels which form the prostatic venous plexus. The plexus receives blood from the dorsal vein of the penis. It communicates with both the vesical and the vertebral plexuses and drains into the internal iliac vein. The arterial blood supply is usually derived from branches of the internal iliac artery, although it may originate from the umbilical artery as well. Just prior to the terminal division of the internal iliac artery into inferior gluteal and internal pudendal branches, the prostatovesical trunk arises which, in turn, yields the artery to the prostate. The lymph drains to the nodes surrounding the pelvic wall, and terminates mainly in the internal iliac nodes, with the sacral and external iliac nodes receiving some of the flow as well.

Nervous innervation is derived from sympathetic fibers of the inferior hypogastric plexus originating at the lumbar 1 and 2 ventral rami. The prostatic nervous plexus also receives communicating branches from the vesical plexus and some sensory fibers derived from the pudendal nerve.

III. HISTOLOGY AND ULTRASTRUCTURE

The prostate is a compound exocrine gland. Its ducts branch profusely. The secretory portions at the ends of the ducts, however, are especially large and contain very wide lumens. Hence, it is common to refer to the prostate as a compound saccular or compound tubuloacinar gland. The 16-32 excretory ducts within a mature prostate each empty into the urethra on the right and left sides of the colliculus seminalis. Most ducts are lined by simple or pseudostratified columnar epithelium which becomes stratified columnar or cuboidal (transitional) at the level of the urethra.

For convenient description, the 'true' prostate or the prostate proper often is divided into two parts: a central and a peripheral zone. The anatomical relationships are seen to advantage when the prostate is sectioned in a plane parallel to the long axis of the ejaculatory ducts. The central zone is shaped like an inverted pyramid: The base of the prostate rests on the neck of the bladder and its apex surrounds the ejaculatory ducts. In this zone, the epithelium is pseudostratified. It contains cuboidal or columnar principal cells and cuneiform basal cells. Occasionally a third cell of intermediate height is crowded into the highly irregular epithelium. The pseudostratification of the cells is pronounced. The large, pale nuclei lie at different levels in the granular, moderately acidophilic cytoplasm. In addition to the conspicuous crowding of epithelial cells, the central zone also is distinguished by larger and more irregular secretory acini than the acini within the peripheral zone. The stroma is compact and very regularly arranged around the glandular units. Ducts from the central zone open into the prostatic urethra at the level of the verumontanum.

Approximately three quarters of the prostate proper is thought to reside in the peripheral zone. The stroma is loosely arranged and moderately irregular whereas the glandular units are regularly arranged and quite uniform in appearance. The epithelium is predominantly simple columnar with an incomplete layer of basal cells (Figure 3). In some prostates it is definitely pseudostratified. However, neither epithelial arrangement is associated with the formation of intralumenal ridges or papillae as in the central zone. Ducts from the peripheral zone open into the lower third of the prostatic urethra.

A transitional zone lies anterior to the peripheral zone and above the verumontanum. Although the epithelium resembles the epithelium of the peripheral zone, the stroma is highly irregular and coarse in texture. The connective tissue and smooth muscle fibers often form incomplete rings parallel to the muscle fibers of the sphincter of the urethra. Benign nodular hyperplasia most commonly is seen in the transition zone.

Above the verumontanum lie many small glands and diverticula from the upper part of the prostatic urethra which give rise to the periurethral portion of the prostate. Nodules which form here are neither as large nor as numerous as nodules formed in the transition zone.

Under normal circumstances, the principal or glandular cells exhibit surface and cytoplasmic polarity. Moderate numbers of filamentous mitochondria, free ribosomes and cisternae of the rough endoplasmic reticulum (RER) reside in the infranuclear cytoplasm. A moderately well developed Golgi, some RER, a few lipid droplets, several membrane bound secretory granules, vacuoles, numerous lysosomes and dense bodies reside in the supranuclear cytoplasm. The apical plasmalemma contains many microvilli and intense aminopeptidase activity (Figure 4). Adjacent principal cells are joined by typical junctional complexes and desmosomes.

Basal cells rest on the basal lamina but do not reach the lumen. They appear to be significantly less specialized than the glandular cells. They exhibit little surface or cytoplasmic polarization although they have abundant tonofilaments and pinocytotic vesicles. Basal cells proliferate in response to a number of normal and abnormal stimuli (Kastendieck and Altenähr 1979).

In all parts of normal glands, both the glandular