superficial bladder cancer, discussed earlier in this chapter. BCG is an attenuated mycobacterial strain that gives rise to a histologic picture indistinguishable from that seen with systemic tuberculosis. However, in the setting of BCG treatment the finding of granulomas in the prostate is of no clinical significance and requires no treatment. Fungal granulomatous prostatitis is typically seen only in immunocompromised hosts. Nonspecific granulomatous prostatitis is relatively common and represents a reaction to secretions from ruptured prostatic ducts and acini. Although some of these men have a recent history of urinary tract infection, bacteria are not seen within the tissue in nonspecific granulomatous prostatitis.

MORPHOLOGY

Acute prostatitis may appear as minute, disseminated abscesses; as large, coalescent focal areas of necrosis; or as diffuse edema, congestion, and boggy suppuration of the entire gland.

In men with symptoms of acute or chronic prostatitis, biopsy or surgical specimens are usually not obtained, because the diagnosis is made on clinical and laboratory findings. In fact biopsy in suspected acute prostatitis is contraindicated, as it may lead to sepsis. It is common in prostate specimens removed surgically to find histologic evidence of acute or chronic inflammation in men with no clinical symptoms of acute or chronic prostatitis. In these instances etiologic infectious agents have yet to be identified. So as not to be confused with the clinical syndromes of acute and chronic prostatitis, these prostate specimens are instead diagnosed using descriptive terms such as "acute inflammation" or "chronic inflammation" and not as "prostatitis."

KEY CONCEPTS

Prostatitis

- Bacterial prostatitis may be acute or chronic; the responsible organism usually is *E. coli* or another gram-negative rod.
- Chronic abacterial prostatitis, despite sharing symptomatology with chronic bacterial prostatitis, is of unknown etiology and does not respond to antibiotics.
- Granulomatous prostatitis has a multifactorial etiology, including infectious and noninfectious causes.

Benign Enlargement

Benign Prostatic Hyperplasia or Nodular Hyperplasia

BPH is the most common benign prostatic disease in men older than age 50 years. It results from nodular hyperplasia of prostatic stromal and epithelial cells and often leads to urinary obstruction. It is characterized by the formation of large, fairly discrete nodules in the periurethral region of the prostate, which, when sufficiently large, compress and narrow the urethral canal to cause partial, or sometimes virtually complete, obstruction of the urethra. Nodular hyperplasia is not considered to be a premalignant lesion.

Incidence. Histologic evidence of BPH can be seen in approximately 20% of men 40 years of age, a figure that increases to 70% by age 60 and to 90% by age 80. There is no direct correlation, however, between histologic changes and clinical symptoms. Only 50% of those who have microscopic evidence of BPH have clinically detectable enlargement of the prostate, and of these individuals, only 50% develop clinical symptoms. BPH is a problem of enormous magnitude, with approximately 30% of white American men older than 50 years of age having moderate to severe symptoms.

Etiology and Pathogenesis. Despite the fact that there are an increased number of epithelial cells and stromal components in the periurethral area of the prostate, there is no clear evidence of increased epithelial cell proliferation in human BPH. Instead, it is believed that hyperplasia mainly stems from impaired cell death, resulting in the accumulation of senescent cells in the prostate. In keeping with this idea, androgens (discussed later), which are required for the development of BPH, not only increase cellular proliferation, but also inhibit cell death.

The main androgen in the prostate, constituting 90% of total prostatic androgens, is dihydrotestosterone (DHT). DHT is formed in the prostate from testosterone through the action of an enzyme called type 2 5α-reductase. This enzyme is located almost entirely in stromal cells; with the exception of a few basal cells, prostatic epithelial cells do not express type 2 5α-reductase. Thus, stromal cells are responsible for androgen-dependent prostatic growth. Type 1 5α-reductase is not detected in the prostate, or is present at very low levels. However this enzyme may produce DHT from testosterone in liver and skin, and circulating DHT may act in the prostate by an endocrine mechanism.

DHT binds to the nuclear androgen receptor (AR) present in both stromal and epithelial prostate cells. DHT is more potent than testosterone because it has a higher affinity for AR and forms a more stable complex with the receptor. Binding of DHT to AR stimulates the transcription of androgen-dependent genes, which includes several growth factors and their receptors. Most important among these are members of the fibroblast growth factor (FGF) family and transforming growth factor (TGF)-β (Chapter 3). FGFs, produced by stromal cells, are paracrine regulators of androgen-stimulated epithelial growth during embryonic prostatic development, and some of these pathways may be "reawakened" in adulthood to produce prostatic growth in BPH. TGF-β serves as a mitogen for fibroblasts and other mesenchymal cells, but inhibits epithelial proliferation. Although the ultimate cause of BPH is unknown, it is believed that DHT-induced growth factors act by increasing the proliferation of stromal cells and decreasing the death of epithelial cells.

MORPHOLOGY

In the usual case of benign prostatic enlargement, the prostate weighs between 60 and 100 gm. Nodular hyperplasia of the prostate originates almost exclusively in the inner aspect of the prostate gland (transition zone). The early nodules are composed almost entirely of stromal cells, and later predominantly

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