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Diseases of the Prostate

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Abstract

The prostate gland is an accessory sex organ found in male goats and other mammals. The prostate gland is an essential reproductive organ in male goats, playing a vital role in semen production and fertility. However, like all living organisms, goats are susceptible to various diseases that can affect the prostate gland and compromise their reproductive health. Some of the diseases affecting goats include prostatitis, benign prostatic hyperplasia (BPH), prostate abscess, and prostate cancer. Prostate pathology could result in decreased reproduction and sperm cell health as it could impair capitation and fertilization potential.

Keywords: disease; goat; buck; prostate; accessory sex organ; reproduction

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19.1 Introduction

The prostate gland is an accessory sex organ that contributes secretions into the seminal fluid, which aids in sperm delivery and fertilization capacity. Two basic types of cells make up the prostate gland: epithelial cells, which produce exocrine secretions, and stromal cells, which provide structure to the gland and help expel secretions into the urethra. The prostate gland in bucks, as in many other mammals, is an essential part of the reproductive system. It is a small, walnut-sized organ located just below the bladder and surrounds the urethra, the tube responsible for transporting urine and semen out of the body. The prostate's main function is to produce and secrete various fluids that help support sperm function and promote successful reproduction (Bazer 2020) Figure 19.1.

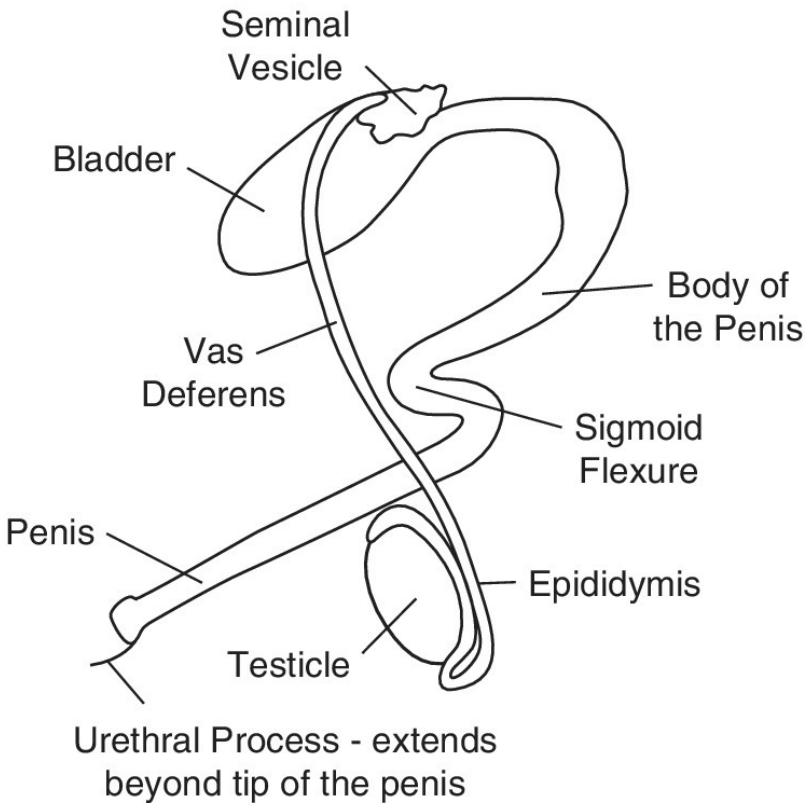

Figure 19.1 Anatomical representation of a buck's reproductive system. *Source:* www.nhptv.org/natureworks/whitetaileddeer.htm.

19.2 Cell Biology

The prostate gland comprises two main types of cells: parenchymal epithelial cells and stromal cells. The parenchymal epithelial cells are responsible for forming the acini and ducts within the gland, and they play a crucial role in secreting prostatic fluid. On the other hand, the stromal cells surround the acini and ducts, providing essential support and structure to the gland (Gauntner and Prins 2018).

19.2.1 Epithelial Cells

The prostate gland's acini and ducts, also known as the parenchyma, are created by three different types of epithelial cells, each with distinct characteristics and functions: basal cells, luminal cells, and neuroendocrine cells. Among these, prostate epithelial cell stem cells are found within the basal cell layer. Surrounding the glandular epithelium, there is a fibromuscular stroma, which aids in the expulsion of prostatic secretions into the urethra during ejaculation (Di Donato et al. 2023).

19.2.1.1 Luminal Epithelial Cells

The prostate gland's exocrine product is generated by secretory luminal cells, which form the inner

lining of the glandular acini. These cells are cuboidal or pseudo-columnar in shape and are positioned atop a layer of basal cells resting on the basement membrane. Their primary function is to secrete various proteins and substances into the lumen of the glands at the apex of the cell (Lew et al. 2023).

These luminal epithelial cells are crucial for producing and releasing prostatic fluid, a vital component of semen. They are situated on the innermost layer of the prostate gland's tubular structures, specifically the prostatic acini or ducts. The prostatic acini are responsible for both synthesizing and storing prostatic fluid. The luminal epithelial cells line the central space (lumen) of these acini, where prostatic fluid accumulates before being released during ejaculation (Di Donato et al. 2023).

19.2.1.1.1 Features of Luminal Epithelial Cells

Luminal epithelial cells possess specific characteristics that make them well suited for their functions in the prostate gland (Di Donato et al. 2023).

- *Columnar shape*: these cells are typically tall and columnar in shape, with elongated nuclei and more abundant cytoplasm compared to basal epithelial cells.
- *Secretory machinery*: luminal epithelial cells are specialized for secretion. They contain numerous organelles, such as Golgi apparatus and secretory vesicles, which are involved in the synthesis and packaging of prostatic fluid components.
- *Apical microvilli*: the apical (top) surface of luminal epithelial cells may have microvilli, which are tiny finger-like projections that increase the cell's surface area for more efficient secretion and absorption.

19.2.1.1.2 Functions of Luminal Epithelial Cells

The luminal epithelial cells of the prostate gland play crucial roles in the production and secretion of prostatic fluid, which serves various functions essential for reproduction (Pitzen and Dehm 2023).

- *Prostatic fluid production*: the main function of luminal epithelial cells is to produce and secrete prostatic fluid. This fluid constitutes a significant portion of semen and contains various substances, including enzymes, citric acid, calcium ions, and prostate-specific antigen (PSA).
- *Contribution to semen*: prostatic fluid contributes to semen's composition which, along with sperm from the testes and seminal fluid from other accessory glands, forms the ejaculate released during copulation. Prostatic fluid provides the necessary nutrients and protection for sperm, enhancing their motility and increasing their chances of successfully fertilizing the female's eggs.

- *Regulation of seminal liquification*: after ejaculation, the prostatic fluid plays a role in the liquification of semen, which initially coagulates to form a gel-like plug in the female reproductive tract. This liquification process allows sperm to disperse more freely, improving their movement within the female reproductive tract.
- *Neutralization of urethral pH*: prostatic fluid contains alkaline substances that help neutralize the acidic environment in the male urethra. This neutralization is important to protect sperm from the potentially harmful acidic conditions and maintain their viability until ejaculation.

19.2.1.2 Basal Epithelial Cells

Basal cells in the prostate gland are nonsecretory epithelial cells that have a flat to cuboidal shape. They can be distinguished from luminal cells based on their expression of specific proteins, including CK5, CK14, and the transcription factor p63. Notably, basal cells do not express PSA or prostatic acid phosphatase (PAP). Additionally, most basal cells do not have androgen receptors (ARs) directly, but may still respond to circulating androgens through paracrine signaling with AR-expressing luminal cells or stromal cells.

In addition to extracellular paracrine signaling, basal and luminal epithelial cells can communicate directly through gap junction proteins, enabling cytoplasmic signaling between these two cell types. This suggests that the unique functions of each cell type are co-regulated by the other. Moreover, junction-like structures are observed between cells in the basal layer, leading some researchers to propose the existence of a blood–prostate barrier similar to the one found in the testis. This barrier might explain why systemically administered antibiotics have poor perfusion into the prostate (Beshiri et al. 2023).

19.2.1.2.1 Functions of Basal Epithelial Cells

While the specific functions of basal epithelial cells are still being investigated, they are believed to serve several important roles in the prostate gland (Beshiri et al. 2023).

- *Stem cell maintenance*: basal epithelial cells are thought to act as stem cells or progenitor cells, responsible for generating and replenishing other cell types within the prostate gland. They have the ability to divide and differentiate into different cell lineages, contributing to the continuous renewal of the prostate tissue.
- *Cellular support*: basal epithelial cells provide support to the glandular cells that produce and secrete prostatic fluid. They help maintain the structural organization of the gland and ensure that the secretory cells are properly arranged for efficient secretion.
- *Hormonal regulation*: these cells may also be involved in responding to hormonal signals that regulate prostate function. Hormones like testosterone and other androgens play a significant role in prostate development and function, and basal epithelial cells may

participate in these hormonal responses.

- *Immune function*: basal epithelial cells might play a role in the immune defense of the prostate gland. They could be involved in detecting and responding to pathogens or foreign substances, helping to protect the gland from infections and inflammation.

19.2.1.3 Epithelial Stem Cells

Prostate stem cells play a crucial role in replenishing the prostate epithelium throughout an individual's life. These stem cells reside within a specialized environment known as the stem cell niche, which is situated within the basal epithelial layer. While in this niche, the stem cells typically remain in a state of relative inactivity (quiescence) until they receive signals from the niche that stimulate their significant potential for proliferation. Our understanding of prostate stem cells has largely been derived from studies in rodent models.

The study of prostate stem cell biology is particularly significant due to the observation that cancer cells share many characteristics with stem cells. Cancer cells possess the ability to divide almost indefinitely, resist apoptosis (programmed cell death), migrate within tissues, and even spread to other tissues, in addition to acquiring altered metabolic states, among other traits.

Prostate stem cells exhibit three fundamental properties: (i) they have a slow growth rate or relative quiescence, (ii) they have a high capacity for replication, and (iii) they can regenerate a prostate-like gland. During development of the prostate gland, the stem cells undergo relatively high levels of proliferation to generate sufficient progeny for the formation of the gland. However, in the adult gland, the stem cells exist in a state of relative quiescence, which is regulated by both intrinsic growth control mechanisms within the stem cells themselves and external cues from the surrounding niche.

Several signaling pathways control the growth and self-renewal decisions of prostate stem cells. These pathways can originate from the stem cells themselves (autonomous) or from other cells within the niche, including progenitor cells and stromal cells (extrinsic). Some of these pathways include bone morphogenic peptide/transforming growth factor-beta (BMP/TGF-beta), wingless-integrated (Wnt)/beta-catenin, fibroblast growth factor (FGF), Notch, Hedgehog, and Ephrin pathways (Beshiri et al. 2023). These signaling pathways play critical roles in maintaining the balance between quiescence and proliferation in prostate stem cells, thereby ensuring the proper functioning of the prostate gland and influencing its potential for cancer development.

19.3 Prostatic Secretions

19.3.1 The Prostate Gland Contributes Secretions to the Seminal Plasma

The sex accessory tissues, such as the prostate, seminal vesicles, bulbourethral glands, and glands of Littre, have a primary function in producing seminal plasma, which is the nongamete portion of semen. Seminal plasma serves as a nutrient-rich, buffered transport medium for sperm during ejaculation and their subsequent journey into the female genital tract. While certain components in

seminal plasma can enhance the fertilizing capacity of sperm, they are not essential for mature spermatozoa to successfully fertilize an egg.

Seminal plasma has a slightly alkaline pH, ranging from 7.2 to 7.8, which helps neutralize the acidic environment of the vagina, creating a more favorable environment for sperm survival. Prostaglandins present in seminal plasma play a role in stimulating the smooth muscle contractions along the female genital tract, aiding in the propulsion of sperm toward the egg.

Several other substances found in seminal plasma contribute to its properties. Zinc and immunoglobulin A (IgA) are two important components with bacteriostatic properties, helping to protect against bacterial infections. Additionally, a range of prostatic proteins is present in seminal plasma, which helps prevent the autoagglutination (clumping) of sperm.

In total, the secretions from the prostate gland account for approximately 25% of the ejaculate volume, which typically ranges from about 1 to 6 ml in human males (Ješeta et al. 2023). The combined contributions of all the sex accessory tissues ensure the successful delivery and survival of sperm within the female reproductive tract, supporting the process of fertilization.

19.3.2 Role of Prostatic Secretions in Coagulation/Liquefaction

Semen coagulates and forms a gelatinous mass soon after ejaculation due to clotting factors produced by the seminal vesicles. Although analogous to blood coagulation, the seminal coagulation process has a unique biochemistry that does not involve prothrombin, fibrinogen, or hematologic clotting factors. Furthermore, the seminal coagulation process is not inhibited by heparin or sodium citrate. Prostate-derived proteolytic enzymes, including seminin, plasminogen activators, and PSA, liquefy the coagulated semen after 15–60 minutes. This liquefaction frees the sperm to advance up the female reproductive tract. Defective or absent secretion of these liquefying factors from the prostate is one cause of reduced male fertility (Ješeta et al. 2023).

19.3.3 Regulation of Prostatic Secretion

The production of seminal plasma, including the prostatic component, is under hormonal control and driven by circulating androgens, which are always present in normal males. In the prostate, circulating testosterone is taken up by prostate cells, converted to dihydrotestosterone (DHT) which binds to luminal cell AR, dimerizes, and translocates to the nucleus. Nuclear AR binds response elements on androgen-regulated genes, initiating gene transcription with subsequent translation of secretory proteins or enzymes whose products are secreted into seminal fluid. Prostatic secretions are also under neural control (Ventura et al. 2002). Both the epithelial and stromal compartments in the prostate are innervated by the autonomic nervous system.

19.3.4 Components of Prostatic Fluid

19.3.4.1 Zinc

The prostate gland contains the highest concentration of zinc of any organ in the human body, as reported by Bertrand and Vladesco in 1921. This elevated zinc level in the seminal plasma, which is about 140 mg/ml, is nearly 100 times higher than the concentration of zinc in the blood serum, according to Eliasson's research in 1977. The exact physiological role of such high zinc

concentrations in the prostate and seminal plasma remains unclear. While the prostate contains numerous zinc-containing metalloenzymes, the observed zinc concentration far surpasses what would be theoretically required for these enzymes to function.

Within the seminal plasma, zinc plays several roles. It acts to stabilize the chromatin within the sperm head, aiding in sperm function and viability. Additionally, zinc binds to semenogelin I and II in the seminal plasma, contributing to the regulation of liquefaction, a process involved in sperm release and movement (Heathcote and Washington 1973; Fair et al. 1976; Jonsson et al. 2005).

Furthermore, zinc serves as an antibacterial agent in both seminal plasma and nonejaculatory prostatic secretions. *In vitro* studies have demonstrated its activity against various Gram-positive and Gram-negative bacteria, as evidenced by research by Radhi et al. (2023). This antibacterial function may play a crucial role in protecting sperm and reproductive health.

Despite these known functions of zinc in the prostate and seminal plasma, the full extent of its physiological significance in these contexts is yet to be fully understood. Ongoing research continues to shed light on the intricate roles of zinc and its implications for male reproductive health.

19.3.4.2 Citric Acid

Citrate, a potent binder of metal ions, is one of the major anions present in human seminal plasma. In ejaculate, the average concentration of citrate is 376 mg/dl, which is 500–1000 times higher than its concentration in blood plasma. The molar concentration of citrate (20 mM) is comparable to the combined concentration of divalent metals in the semen, which includes calcium (7 mM), magnesium (4.5 mM), and zinc (2.1 mM). The primary source of citrate in seminal plasma is the prostate, while seminal vesicle secretions contribute to a much lower concentration of citrate, approximately 100-fold less. The elevated levels of citrate have been associated with a decreased ability of prostatic mitochondria to oxidize citrate, leading to an imbalance between citrate production and oxidation. Researchers measured citrate and isocitrate levels and found that the prostate has a ratio of 33:1, whereas other tissues demonstrated ratios of 10:1. This finding suggests that reduced aconitase activity may be responsible for the unusually high citrate levels in prostatic secretions (Yun et al. 2023).

19.3.4.3 Sodium, Potassium, Calcium, Magnesium, and Chloride

Although seminal plasma contains calcium and magnesium in higher concentrations than other body fluids, the relative contribution of the prostate to these levels has not been established. It is known, however, that the concentration of sodium, potassium, calcium, magnesium, and chloride within prostatic fluid varies between individuals and states of wellness or disease. This is in part a passive response to varied levels of citrate secretion in prostatic fluid during states of disease (Rodríguez-Díaz et al. 2023).

19.3.4.4 Spermine

Polyamines are small, positively charged organic molecules that have two or more primary amino groups. These molecules are found in all eukaryotic cells, where they have pleiotropic effects on a variety of physiological processes including cell proliferation. Spermine, so named as a polyamine

that was first discovered in semen, is present in seminal plasma at concentrations of 50–350 mg/dl and imparts a unique odor to semen. The prostate gland has the highest concentration of spermine in the human body and is the primary source of this polyamine in seminal plasma. The enzyme ornithine decarboxylase (ODC) is the rate-limiting enzyme in the synthesis of polyamines and spermine. The expression of ODC is increased in benign prostatic hyperplasia (BPH) tissue, which suggests a possible role for polyamines in the pathogenesis of this disease. At physiological pH, spermine has four positive charges that bind strongly to acidic or negatively charged molecules such as phosphate ions, nucleic acids, or phospholipids.

Spermine is generated via a series of enzymatic reactions that use other polyamines as substrates, proceeding from ornithine to putrescine to spermidine to spermine. Spermine is oxidized enzymatically by diamine oxidase, which is found in the seminal plasma. The aldehyde products from this reaction are very reactive and toxic to both sperm and bacteria. This is one reason why prolonged exposure of sperm to seminal plasma will reduce its fertilizing capacity (Prylutskyi et al. 2023).

19.3.4.5 Prostaglandins

In 1934, von Euler coined the term *prostaglandins* to describe the active components in seminal plasma on the assumption that they were produced by the prostate. Over 20 years later, Eliasson determined that the majority of prostaglandins originate from the seminal vesicles, with the prostate gland's contribution being minimal (Eliasson 1959). Nevertheless, the name stands to this day.

Prostaglandins are expressed throughout the body but in humans, the highest concentrations by far are found in the seminal vesicles. The seminal plasma contains 15 different prostaglandins at a concentration of 100–300 mg/ml. Prostaglandins are 20-carbon hydroxyl fatty acids containing a cyclopentane ring and two side chains. They are classified into four major groups (A, B, E, and F) based on the structure of the cyclopentane ring and given a number based on the structure of the side chain (e.g., PGE3). The E group of prostaglandins predominates in the male reproductive tract, while the F group predominates in the female.

Prostaglandins have a variety of potent proposed physiological effects in the male and are involved in erection, ejaculation, sperm motility, and testicular and penile contractions. Additionally, seminal fluid prostaglandins deposited in the vagina affect cervical mucus, vaginal secretions, and uterine contractions (Hoxha et al. 2023).

19.3.4.6 Cholesterol and Lipids

The human prostate contributes to the lipid fraction of seminal plasma, which contains 185 mg/dl of total lipids, 103 mg/dl of cholesterol, and 83 mg/dl of phospholipids. The phospholipids have been further characterized as 44% sphingomyelin, 12.3% ethanolamine plasmalogen, and 11.2% phosphatidylserine. This ratio of cholesterol to phospholipid helps stabilize the sperm against temperature and environmental shock (Goyal and Saxena 2023b).

19.3.4.7 Immunoglobulins

Immunoglobulins are found in the seminal plasma at levels lower than in blood. Specifically, IgG

is measured from 7 to 22 mg/dl and IgA from 0 to 6 mg/dl. IgM has also been detected in the seminal plasma at very low levels (Gahankari and Golhar 1993). Given the lower levels of immunoglobulins, it is theorized that these may simply be exudates, but IgA has been localized more so to the bulbourethral glands and suggests an immunological component to the bulbourethral gland function. IgG and IgA are likely secreted from the prostate (Carvalho et al. 2023).

19.3.4.8 Acid Phosphatase

Acid phosphatase activity is more than 200 times more abundant in the prostate than any other tissue. PAP is a glycoprotein dimer with seminal plasma levels of 0.3–1 g/l. The substrate for PAP in the seminal plasma may be phosphorylcholine phosphate, which is rapidly hydrolyzed by the enzyme. However, the physiological significance of the high levels of PAP and their function are not well understood. Serum acid phosphatase concentration was once widely measured as a biomarker for metastatic prostate cancer but this has been replaced by the more sensitive and specific assay for PSA (Ngo et al. 2023).

19.3.4.9 Prostate Specific Antigen

Prostate specific antigen is a 33 kD glycoprotein that acts as a serine protease and is produced almost exclusively in prostate epithelial cells, PSA is involved in lysing the ejaculatory clot with semenogelin as its substrate. The PSA gene (hKLK3) is a member of the kallikrein family which are all located on chromosome 19. Expression of PSA is dependent upon androgens.

Clinically, PSA is used as an important serum marker for prostate cancer and prostate disease since its presence in the circulation indicates a breakdown in the epithelial/basement membrane barrier. Unfortunately, while PSA is organ specific, it is not cancer specific and is found in the serum of patients with BPH as well as prostatitis. PSA is found in seminal plasma in concentrations from 0.5 to 5 mg/ml whereas PSA in serum of men 50–80 years of age without prostate disease is 1000-fold less at 1.0–4.0 ng/ml. The serum level of PSA in men with prostate cancer is generally elevated (>4.0 ng/ml), but not until its level is >10 ng/ml does this measurement suggest specificity for prostate cancer.

As prostate cancer cells remain A -dependent, even in the absence of androgens, circulating levels of PSA in patients with metastatic disease can reach into the hundreds and monitoring levels over time can be a useful indicator of progression and relapse after treatment failure (Unuma et al. 2023).

19.4 Diseases of the Prostrate

Diseases of the prostate in goats can affect their reproductive health and overall well-being. While goats are generally hardy and resistant to many diseases, they are not immune to prostate-related issues. Here are some common diseases of the prostate that can affect goats (Zachary and McGavin 2012).

19.4.1 Prostatitis

Prostatitis is inflammation of the prostate gland, and it can occur in goats due to various reasons,

including bacterial infections. Infections may ascend from the urinary tract or be introduced through the bloodstream. Symptoms of prostatitis in goats include difficulty urinating, frequent urination, blood in the urine, and discomfort in the hindquarters.

19.4.2 Benign Prostatic Hyperplasia (BPH)

Benign prostatic hyperplasia is a noncancerous enlargement of the prostate gland, commonly seen in aging goats. As goats get older, hormonal changes can lead to the growth of prostate tissue, causing the gland to enlarge. BPH can lead to urinary obstruction and difficulty in passing urine, leading to discomfort and distress for the goat.

19.4.3 Prostatic Abscesses

Prostatic abscesses can develop as a result of bacterial infections in the prostate gland. These abscesses are pus-filled pockets that can cause severe pain, difficulty urinating, and systemic signs of illness such as fever and lethargy.

19.4.4 Prostate Cancer

Prostate cancer is a relatively rare condition in goats but can occur. Tumors may develop in the prostate gland, leading to various urinary and reproductive issues. Unfortunately, prostate cancer in goats often has a poor prognosis.

19.4.5 Prostate Calculi

Prostate calculi are mineral deposits that can form within the prostate gland or urinary tract. They can obstruct the urethra, making it difficult for the goat to urinate and leading to potential urinary blockages and related complications.

19.4.6 Prostatic Cysts

Prostatic cysts are fluid-filled sacs that can develop within the prostate gland. They may cause discomfort, pain, and issues with urination, especially if they grow large enough to compress surrounding structures.

19.5 Conclusion

The prostate gland is a crucial organ in the reproductive health of male goats, responsible for semen production and fertility. Various diseases can afflict the prostate gland, such as prostatitis, BPH, prostate abscess, and even prostate cancer. Early detection and proper treatment are essential to ensure the overall well-being and productivity of male goats. Goat farmers must be vigilant, implement preventive measures, and collaborate with veterinarians to maintain the health of their herds and secure the future of their goat farming endeavors.

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