Prostate embryology, anatomy and physiology

Embryology
5 paired epithelial buds project posteriorly from urethra into USM at 13-16 weeks under the influence of DHT
Top pairs derived from mesoderm – form TZ/periurethral zones
  Low secretory activity
  Apoptosis
Lower pairs derived from endoderm – PZ
Outer duct - high mitosis, low secretion
Mid duct – less mitosis, high secretion
Inner duct – no mitosis, no secretion, apoptosis

Stromal-epithelial interaction
Prostate development requires presence of surrounding stroma
Determined by classic work by Jerry Cunha 1983
  Urogenital sinus mesenchyme (USM) induces prostate epithelial differentiation from adult bladder epithelium
  Absolute requirement for USM androgen receptor (not present in testicular feminisation)
Further growth of prostatic epithelium regulated by interaction with basement membrane and stromal cells - defect in stromal component responsible for inhibition of cell proliferation and development of BPH

Anatomy
70% glandular (simple columnar or cuboidal epithelium); 30% fibromuscular stroma. Glandular elements:
- 70% peripheral zone (70% cancers)
- 25% central zone (5-10% cancers)
- 5-10% transitional zone lateral lobes (20% cancers)
- 1% periurethral zone middle lobe

NB. urethral angle (typically 35') divides periurethral zone from TZ (see below)

Central zone - Wolffian structures – under influence of T

Remaining prostate – urogenital sinus mesenchyme – under influence of DHT
Pre-prostatic sphincter
Signet ring, deficient posteriorly (remember anterior fibromuscular stroma)
Innervation of sphincter predominantly
adrenergic and cholinergic, with others (NANC):
Cholinergic
  epithelial secretion
Adrenergic
  98% in stroma, not epithelium
  90% α1 (60% α1a)
  10% α2
  smooth muscle contraction
Neuroendocrine cells
  Serotonin, calcitonin, TSH,
  somatostatin
  regulation of secretion & cell
growth
NANC
  Substance P, neuropeptide Y,
  encephalins, VIP
  Function unknown
<table>
<thead>
<tr>
<th>Bladder Neck</th>
<th>Preprostatic Sphincter</th>
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<tbody>
<tr>
<td>Both sexes</td>
<td>Males</td>
</tr>
<tr>
<td>At bladder neck</td>
<td>Supravermontanal</td>
</tr>
<tr>
<td>Cholinergic innervation</td>
<td>Adrenergic innervation</td>
</tr>
<tr>
<td>Continence mechanism</td>
<td>Genital sphincter</td>
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</tbody>
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Endocrinology and physiology

Prostate function unknown - secretory
Testosterone required for normal function
Permissive role for growth; androgen withdrawal = prostate involution
Majority of serum testosterone from testis – unbound T bioavailable form
DHT formed within prostate epithelial cells – 40x more active vs. T
DHT diffuses to stroma (most of the androgen receptors; paracrine effect)
Stromal nuclei produce growth factors
Growth factors drive epithelial cells
Stimulatory
  bFGF, KGF (FGF-7) and EGF* and IGF (80%)
  TGFα (20%)
Inhibitory
  TGFβ

* EGF believed to be dominant factor regulating prostate epithelial growth

Prostatic secretion
Proteins and non-proteins (see below)
Zinc maintains quaternary structure of sperm chromatin
PSA aids liquefaction of seminal fluid
Citrate thought to act as buffer for seminal fluid (~750x conc. vs. other tissues)

<table>
<thead>
<tr>
<th>Proteins</th>
<th>Non proteins</th>
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<tbody>
<tr>
<td>Acid phosphatase</td>
<td>Citrate</td>
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<tr>
<td>PSA</td>
<td>Spermine</td>
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<tr>
<td>Leucine aminopeptidase</td>
<td>Spermidine</td>
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<tr>
<td>Diamine oxidase</td>
<td>Putrescine</td>
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<tr>
<td>B Glucuronidase</td>
<td>Zinc</td>
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<tr>
<td>Plasminogen activator</td>
<td>Myoinositol</td>
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<tr>
<td>Complement C3 and C4</td>
<td>Cholesterol</td>
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<td>Transferrin, transferritin</td>
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<tr>
<td>Growth factors</td>
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<td>Annexin 1</td>
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