# Endocrinology of the Epididymis and Sperm Maturation

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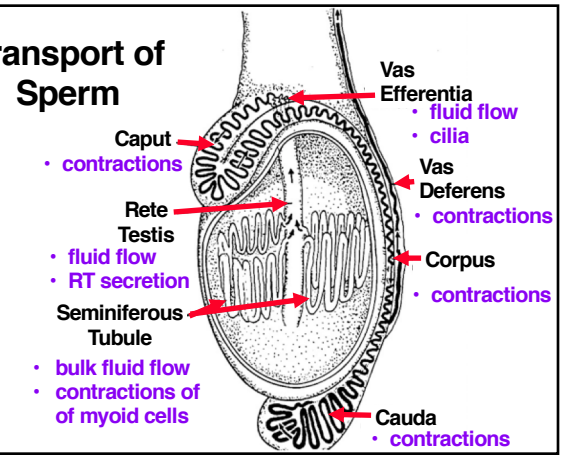
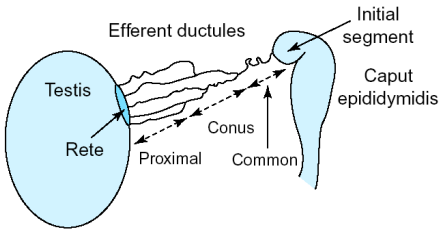
References: The Physiology of Reproduction, Knobil and Neill, 2006; Chapter on the Epididymis by Robaire

## Transport of Sperm

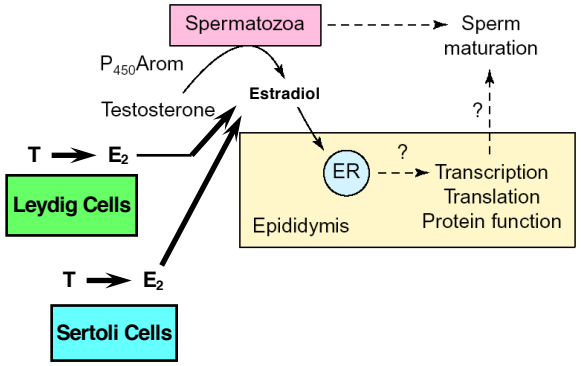


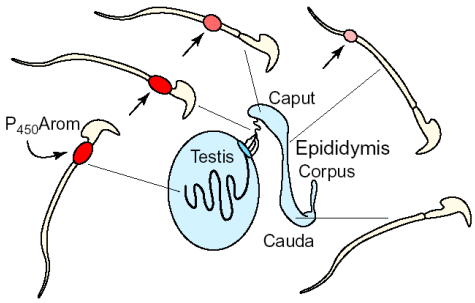

## Vas Efferentia




## Vas Efferentia

- 10 - 15 tubes
- Cilia present
- Site of fluid absorption (90%)
  - Concentrates sperm
- Highest number of estrogen receptors in male

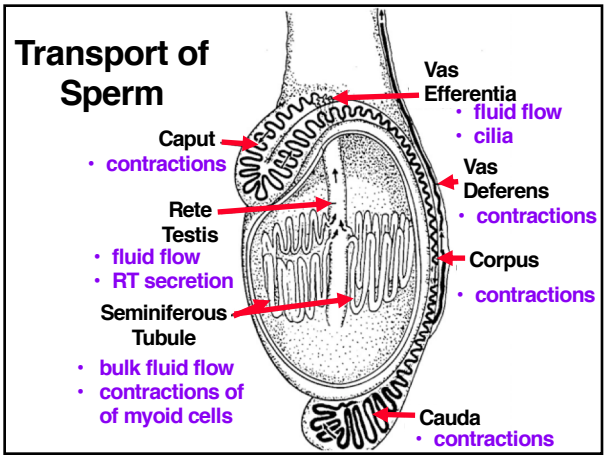


## Vas Efferentia

- 10 - 15 tubes
- Cilia present
- Site of fluid absorption
  - Concentrates sperm
- Highest number of estrogen receptors in male
  - $E_2$ most likely from sperm
  - $ER_\alpha KO$ mouse sterile
    - Fluid accumulation, sperm do not concentrate
    - $E_2$ regulates the process of fluid absorption

## Transport of Sperm

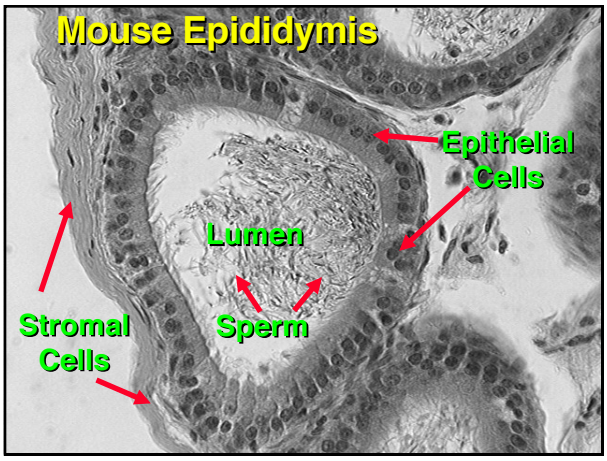



## Epididymis

- Originally not thought to affect sperm but was only a holding tube.
- Requires 10-14 days for sperm to transit
  - Sperm maturation was only an aging effect
- Numerous studies have shown though that the epididymis is actively involved in sperm maturation.

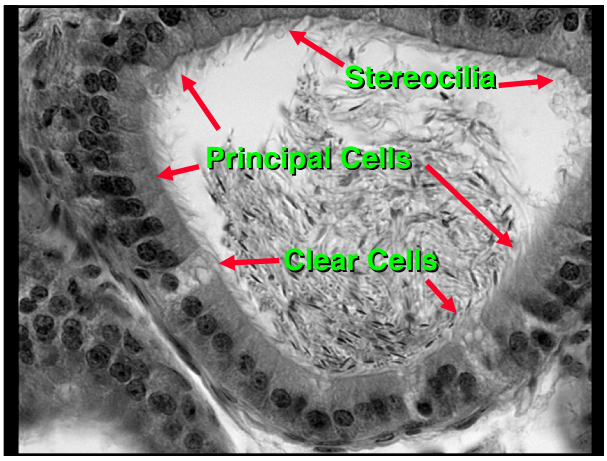
## Epididymal Structure

- caput
  - receives sperm from efferent ducts
- corpus
  - connects caput to cauda
- cauda
  - stores sperm before ejaculation




## Epithelial Cells of the Epididymis

- Surrounded by stromal layer
- Epithelium - Psuedostratified
  - Principal cells (59%)
    - tall columnar and with stereocilia
    - secretion, transport and absorption
    - the height varies with epididymal segment
    - only cells that express 5α-Reductase ($5\alpha\text{-}R_x$)

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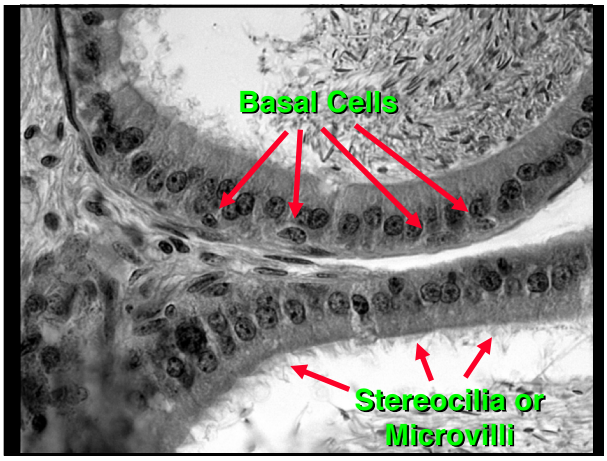
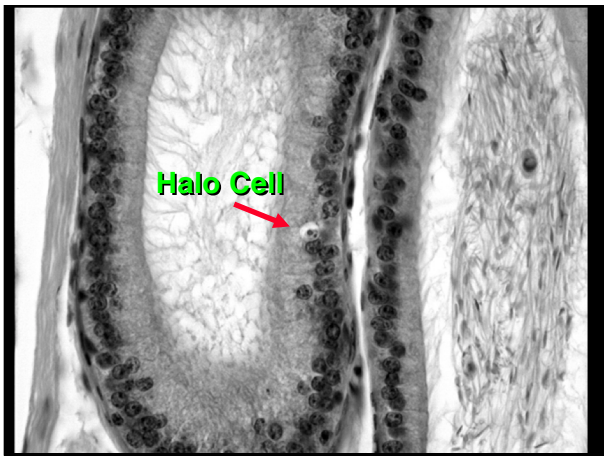
    - secretion, transport and absorption
    - the height varies with epididymal segment
    - only cells that express $5_{\alpha}$-Reductase ($5_{\alpha}$-$R_x$)
  - Clear cells (10%)
    - large pale cells that span epithelium
    - vesicles in apical region, lysosomes in midregion, lipid droplets near base
    - appear to remove material from lumen




## Epithelial Cells of the Epididymis (cont.)

- Basal cells (27%)
  - small elongated cells found throughout
  - potential role in detoxification
- Halo(1-3%)
  - found throughout
  - in various positions but do not span the epithelium
  - are monocytes or lymphocytes (part of immune system)
  - function is unclear
- Blood-Epididymis Barrier
  - tight junctional network among principal cells is extensive

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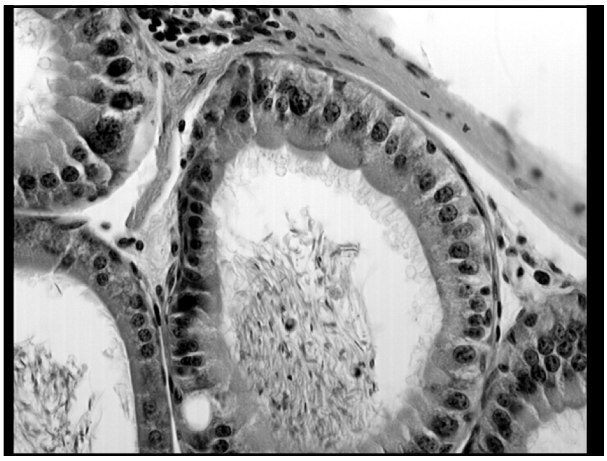
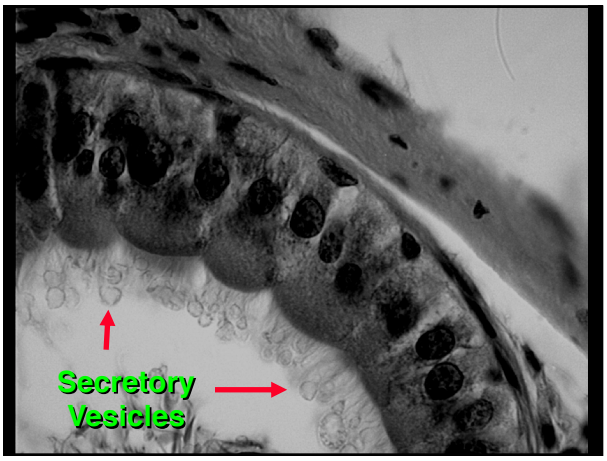





## Functions of the Epididymis

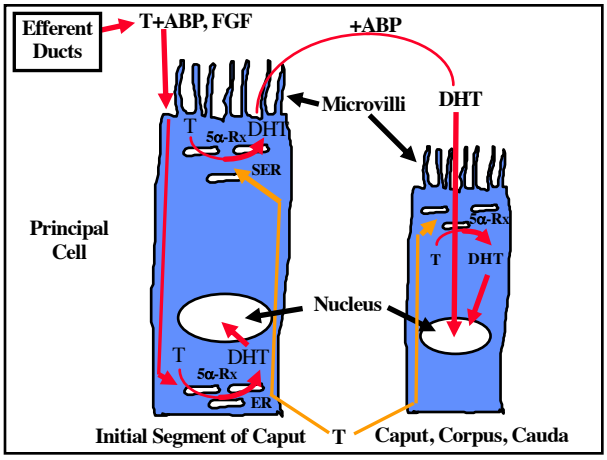
- Maturation of Sperm (Secretion)
  - motility
  - fertility
- Protection
- Concentration (Absorption)
- Storage
- Transport

## Regulation of Epididymal Function

- Absolute requirement for Androgens
  - Testosterone (T), Dihydrotestosterone (DHT)
- Testicular Androgens and Paracrine Factors
  - Caput
    - ligation of efferent ducts leads to decreased function of caput
      - change in the distribution of 5α-$R_x$
    - androgen withdrawal, followed by androgen administration (return to normal levels) does not completely restore caput function

    ⇒Paracrine factors in the testicular fluid influence androgen effects (lumicrine)

B. Robaire and R.S. Viger. BOR 52:226-236 (1995)




## Segment-Specific Control of $5_\alpha$-$R_x$

- Initial segment of Caput
  - abundant expression
  - need to rapidly convert massive amounts of T to DHT
    - DHT required to maximally stimulate androgen-dependent genes
  - T bound to ABP as it enters initial segment
    - ABP turns on expression of the basal-infranuclear $5_\alpha$-$R_x$
    - T converted to DHT, principally regulates effects within principal cells
  - FGF also in fluid of initial segment
    - FGF also turns on expression of basal-infranuclear $5_\alpha$-$R_x$
  - Vascular T effects apical expression of 5α-$R_x$

## Segment-Specific Control of $5_\alpha$-$R_x$ (cont.)

- Proximal and Distal Caput, Corpus, Cauda
  - Vascular T effects apical expression of $5_\alpha$-$R_x$

## Hormonal and Paracrine Control of Epididymal Function

- Caput
  - Initial
    - luminal T + ABP, FGF
    - vascular T
  - Proximal, Distal
    - luminal DHT
    - vascular T
- Corpus, Cauda
  - Proximal, Distal
    - luminal DHT
    - vascular T

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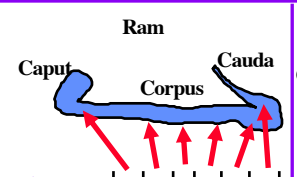
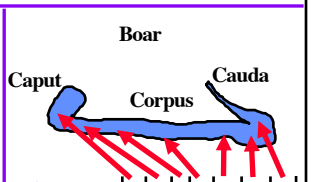
## Acquisition of Sperm Motility and Fertility




| Motile Sperm (%) | 1 | 5 | | 44 | 70 | 81 |
|---|---|---|---|---|---|---|
| Oocytes with bound sperm(%) | 50 | 100 | | 100 | | |
| Preg Rate (%) | 0 | 8 | 12 | 54 | 78 | 80 |
| Preg Maint. (%) | | 0 | 0 | 77 | 86 | 100 |




| Motile Sperm (%) | 0 | 2 | 5 | 17 | 31 | 55 | 55 |
|---|---|---|---|---|---|---|---|
| Hamster Oocytes with bound sperm(%) | 0 | 0 | 5 | 83 | 100 | 100 | 100 |
| Preg Rate (%) | 8 | | | 26 | 25 | 50 | 79 |

## Functions of the Epididymis

- Maturation of Sperm (Secretion)
  - motility
  - fertility
- Protection
- Concentration
- Storage
- Transport

## Protection

- Blood-epididymis barrier
- Role of epididymal proteins
  - Protease inhibitors
  - Compliment mediated cell lysis inhibitor, clusterin
- Oxidative stress
  - superoxide dismutase, catalase, glutathione peroxidase

## Functions of the Epididymis

- Maturation of Sperm (Secretion)
  - motility
  - fertility
- Protection
- **Concentration**
- Storage
- Transport

## Concentration

- **Absorption of fluid in the initial and proximal caput**
  - **principal cells are involved**
    - **take on shape of water transporting epithelium such as in the kidney**
    - **tall columnar epithelium**
    - **presence of tight junctions among principal cells to form blood-epididymal barrier**

## Functions of the Epididymis

- Maturation of Sperm (Secretion)
  - motility
  - fertility
- Protection
- Concentration
- **Storage**
- Transport

## Energy Metabolism

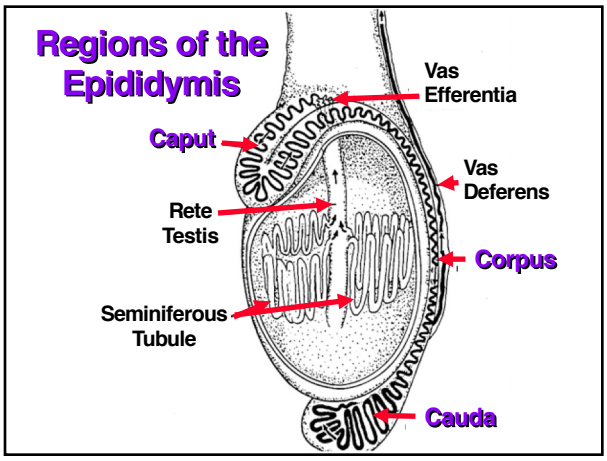
- **Lipids**
  - **ability to utilize lipids develops during epididymal maturation**
  - **carnitine is taken up by sperm during epididymal passage**
  - **metabolism of lipid leads to acetylation of carnitine that is then transported into mitochondria and is involved in respiration.**
  - **lipids utilized are likely not of structural importance**
  - **there is uptake of fatty acids secreted by the principal cells**

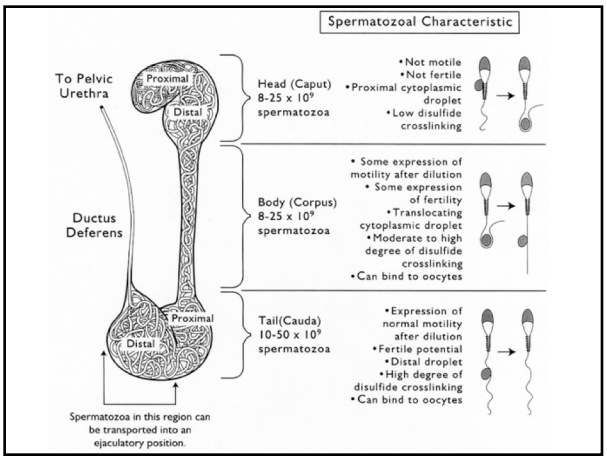
## Energy Metabolism

- **Lactate**
  - **secreted by epithelial cells and can be utilized by sperm**
  - **was primary energy source for spermatids**
- **Glucose**
  - **usually not present**
- **Amino acids**
  - **don't appear to use very much**

## Functions of the Epididymis

- Maturation of Sperm (Secretion)
  - motility
  - fertility
- Protection
- Concentration
- Storage
- **Transport**
  - **fluid flow**
  - **muscle contractions**


Regions of the Epididymis
Vas Efferentia
Caput
Vas Deferens
Rete Testis
Corpus
Seminiferous Tubule
Cauda


Spermatozoal Characteristic
To Pelvic Urethra
Proximal
Distal
Ductus Deferens
Proximal
Distal
Spermatozoa in this region can be transported into an ejaculatory position.
Head (Caput) 8-25 x 10⁹ spermatozoa
•Not motile
•Not fertile
•Proximal cytoplasmic droplet
•Low disulfide crosslinking
Body (Corpus) 8-25 x 10⁹ spermatozoa
• Some expression of motility after dilution
• Some expression of fertility
•Translocating cytoplasmic droplet
•Moderate to high degree of disulfide crosslinking
•Can bind to oocytes
Tail(Cauda) 10-50 x 10⁹ spermatozoa
•Expression of normal motility after dilution
•Fertile potential
•Distal droplet
•High degree of disulfide crosslinking
•Can bind to oocytes