



## **Abnormalities and toxicity in the head of the epididymis: effects on testis and epididymal sperm**

*Anomalias e toxicidade na cabeça do epidídimo: efeitos nos testículos e no esperma epididimário*

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The head of the epididymis receives spermatozoa from the rete testis and plays an important role in preparing sperm for storage in the more distal regions prior to ejaculation. Spermatozoa leave the seminiferous tubule surrounded by an abundance of luminal fluids and travel through rete testis chambers, become more concentrated in the lumen of the numerous, highly convoluted efferent ductules and finally enter the long, single coiled tubule of the epididymis, where sperm are further modified by secretions and reabsorption during their storage prior to ejaculation via the vas deferens. These various regions of the male reproductive tract are typically studied as separate organs, as they have distinct epithelia and physiological activities. However, gross morphological descriptions of the regions adjacent to the testis often are not adequate to explain pathophysiological changes that are observed in certain diseases and after various toxicological exposures or in gene knockout mice. Efferent ductules are typically excluded from the epididymal head. However, in larger mammals, coils of the efferent ductules occupy a major portion of the head of the epididymis or proximal region of the caput epididymis (sometimes called initial segment). In rodents, most of the efferent ductules are located outside the connective tissue capsule that surrounds the head of the epididymis. There are also other major design differences that have potential to influence pathophysiological responses of this region, such as multiple efferent ductules entering independently into the initial segment epididymis in larger mammals, while all ductules merge into a single efferent duct before entering the epididymis in rodents. One of the major developmental anomalies associated with the epididymal head is the formation of blind-ending ducts, which in larger mammals can result in sperm granulomas. Efferent ductules and initial segment epididymis play a major role in the reabsorption of luminal fluids, resulting in a significant increase in the concentration of sperm. Loss of this resorptive activity has been noted in estrogen receptor alpha (ESR1) disruption and in certain toxicology models, which results in fluid backpressure and seminiferous tubular atrophy, as well as epididymal sperm inhibition leading to male infertility. Disruption of spermatogenesis and passage of epididymal sperm is also caused by obstruction of the ductal lumens, as seen following exposure to the fungicide Benomyl. All of these toxicities and developmental deformities have varying degrees of feedback effects on the testis, but all lead to serious disruption of sperm maturation. However, long-term consequences appear to depend upon important species differences in efferent ductule anatomy. Unfortunately, these abnormalities often go underreported because the collection of tissues from efferent ducts and head of the epididymis is easily overlooked in routine pathology.

**Keywords:** epididymis, estrogen, ion transport, occlusion, testis, toxicity.

**Palavras-chave:** epidídimo, estrógeno, testículo, toxicidade.