Prostate – Inflammation, [Acute, Suppurative, Chronic, Chronic-active, Granulomatous]

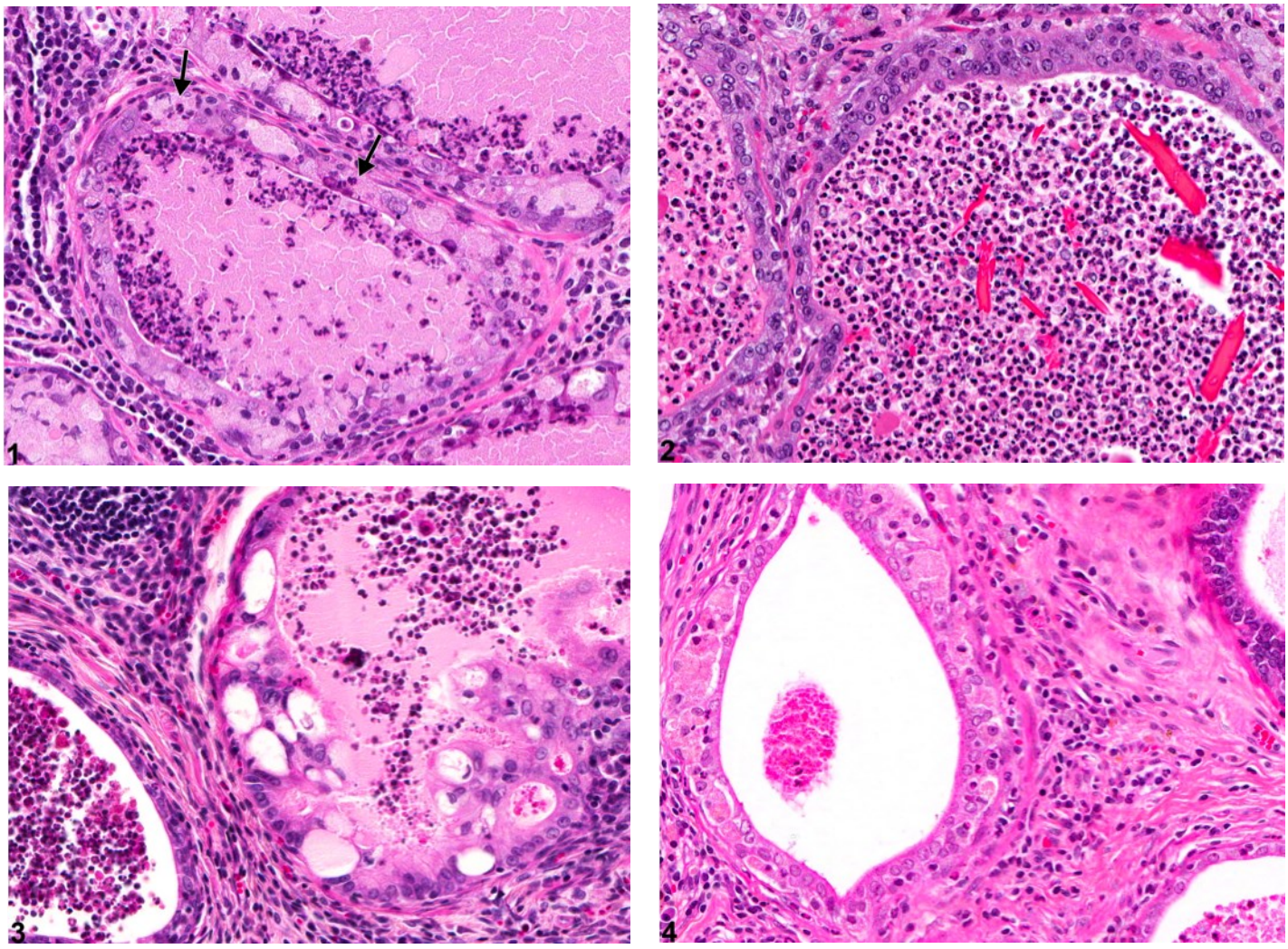
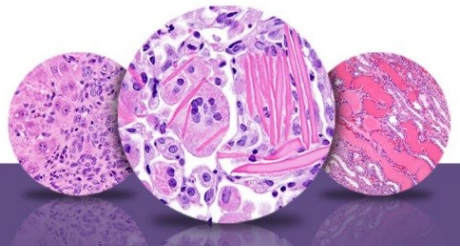


Figure Legend: Figure 1 Prostate - Inflammation. Arrows indicate neutrophils passing through the acinar mucosa in a male F344/N rat from a chronic study. **Figure 2** Prostate - Inflammation. Suppurative inflammation of the prostate in a male F344/N rat from a chronic study. **Figure 3** Prostate - Inflammation. Inflammation of the prostate associated with epithelial degeneration in a male F344/N rat from a chronic study. **Figure 4** Prostate - Inflammation. Chronic inflammation of the prostate in a male F344/N rat from a chronic study.

Comment: Prostatitis is a common microscopic observation in rodents observed during the safety and chronic toxicity assessments of chemicals. Prostatitis can be acute (Figure 1), suppurative (Figure 2),



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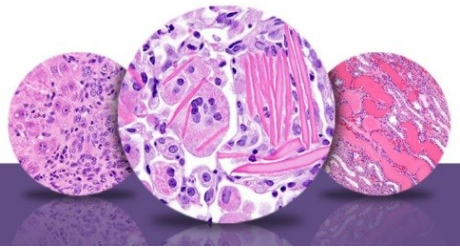
chronic-active with neutrophils in acinar lumens and mononuclear cells in the interstitium (Figure 3), or chronic with interstitial fibrosis (Figure 4). The acinar lining epithelium may remain intact (Figure 1) or have evidence of degeneration, necrosis, or squamous metaplasia (Figure 2 and Figure 3). Neutrophils gain access to the acinar lumen by passing through the acinar mucosa (Figure 1, arrows). Inflammation can occur in any lobe of the prostate or involve multiple lobes. Chemical agents causing prostatitis in rodents are rare. However, prostatitis has been recorded in rats exposed to estrogenic agents perinatally.

In rats, transplacental exposure of atrazine, an agrochemical, results in prostatitis in the adult offspring. It is thought that estradiol-induced inflammation in the rat lateral prostate is mediated, at least in part, by the release of prolactin from the pituitary gland. Prostatic inflammation was demonstrated by experimental hyperprolactinemia induced by chronic administration of sulpiride, a dopamine D2 antagonist with antipsychotic effect.

NTP studies have five standard categories of inflammation: acute, suppurative, chronic, chronic-active, and granulomatous. In *acute inflammation*, the predominant infiltrating cell is the neutrophil, though fewer macrophages and lymphocytes may also be present. There may also be evidence of edema or hyperemia. The neutrophil is also the predominant infiltrating cell type in *suppurative inflammation*, but they are aggregated, and many of them are degenerate (suppurative exudate). Cell debris from both the resident cell populations and infiltrating leukocytes, proteinaceous fluid containing fibrin, fewer macrophages, occasional lymphocytes or plasma cells, and, possibly, an infectious agent may also be present in the exudate. Grossly, these lesions would be characterized by the presence of pus. The tissue surrounding the exudate may have fibroblasts, fibrous connective tissue, and mixed inflammatory cells, depending on the chronicity of the lesion. Lymphocytes predominate in *chronic inflammation*. Lymphocytes also predominate in *chronic-active inflammation*, but there are also a significant number of neutrophils. Both lesions may contain macrophages. *Granulomatous inflammation* is another form of chronic inflammation, but this diagnosis requires the presence of a significant number of aggregated, large, activated macrophages, epithelioid macrophages, or multinucleated giant cells.



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Recommendation: Prostatitis and its exacerbation by chemical agents should be graded and classified. The affected lobe(s) should be identified if possible and indicated in the tissue identification (e.g., prostate, lateral lobe - inflammation, suppurative, moderate). When paired lobes are affected, the diagnosis should indicate the inflammation is bilateral, and the severity grade should be based on the more severely affected lobe. Associated changes such as metaplasia or degeneration should not be diagnosed unless warranted by their extent and severity.

References:

Boorman GA, Elwell MR, Mitsumori K. 1990. Male accessory sex glands, penis, and scrotum. In: Pathology of the Fischer Rat: Reference and Atlas (Boorman GA, Eustis SL, Elwell MR, Montgomery CA, MacKenzie WF, eds). Academic Press, San Diego, 419-428.
Abstract: http://www.ncbi.nlm.nih.gov/nlmcatalog/9002563

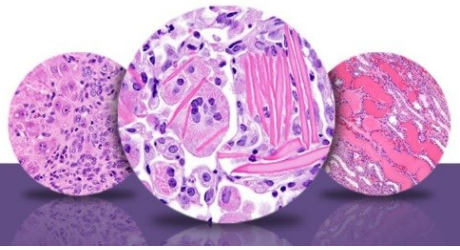
Bosland MC. 1992. Lesions in the male accessory glands and penis. In: Pathobiology of the Aging Rat, Vol 1 (Mohr U, Dungworth DL, Capen CC, eds). ILSI Press, Washington, DC, 443-467.
Abstract: http://catalog.hathitrust.org/Record/008994685

Creasy D, Bube A, de Rijk E, Kandori H, Kuwahara M, Masson R, Nolte T, Reams R, Regan K, Rehm S, Rogerson P, Whitney K. 2012. Proliferative and nonproliferative lesions of the rat and mouse male reproductive system. Toxicol Pathol 40:40S-121S.
Abstract: http://www.ncbi.nlm.nih.gov/pubmed/22949412

Dixon D, Heider K, Elwell MR. 1995. Incidence of nonneoplastic lesions in historical control male and female Fischer-344 rats from 90-day toxicity studies. Toxicol Pathol 23:338-348.
Abstract: http://www.ncbi.nlm.nih.gov/pubmed/7659956

Fabien VC, Slomianny C, Carpentier F, Bourhis XL, Ahidouch A, Croix D, Legrand G, Dewailly E, Fournier S, Cousse H, Authie D, Raynaud J, Beauvillain J, Dupouy J, Prevarskaya N. 2001. Effects of hyperprolactinemia on rat prostate growth: Evidence of androgeno-dependence. Am J Physiol Endocrinol Metab 280:E120-E129.
Abstract: http://www.ncbi.nlm.nih.gov/pubmed/11120666

Gordon LR, Majka JA, Boorman GA. 1996. Spontaneous nonneoplastic and neoplastic lesions and experimentally induced neoplasms of the testes and accessory sex glands. In: Pathobiology of the Aging Mouse, Vol 1 (Mohr U, Dungworth DL, Capen CC, Carlton WW, Sundberg JP, Ward JM, eds). ILSI Press, Washington, DC, 421-441.
Abstract: http://catalog.hathitrust.org/Record/008994685



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References:

Rayner JL, Enoch RR, Wolf DC, Fenton SE. 2007. Atrazine-induced reproductive tract alterations after transplacental and/or lactational exposure in male Long-Evans rats. Toxicol Appl Pharmacol 218:238-248.
Abstract: http://www.ncbi.nlm.nih.gov/pubmed/17204298

Stoker TE, Robinette CE, Britt BH, Laws SC, Cooper RL. 1999. Prepubertal exposure to compounds that increase prolactin secretion in the male rat: Effects on the adult prostate. Biol Reprod 61:1636-1643.
Abstract: http://www.ncbi.nlm.nih.gov/pubmed/10570013

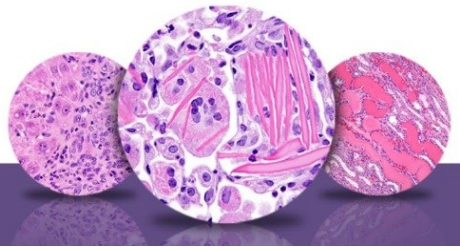
Stoker TE, Robinette CL, Cooper RL. 1999. Maternal exposure to atrazine during lactation suppresses suckling-induced prolactin release and results in prostatitis in the adult offspring. Toxicol Sci 52:68-79.
Abstract: http://toxsci.oxfordjournals.org/content/52/1/68.abstract

Stoker TE, Robinette CE, Cooper RL. 1999. Perinatal exposure of estrogenic compounds and the subsequent effects on prostate of the adult rat: Evaluation of inflammation in the ventral and lateral lobes. Reprod Toxicol 3:463-472.
Abstract: http://www.ncbi.nlm.nih.gov/pubmed/10613394

Suwa T, Nyska A, Peckham JC, Hailey JR, Mahler JF, Haseman JK, Maronpot RR. 2001. A retrospective analysis of background lesions and tissue accountability for male accessory sex organs in Fischer-344 rats. Toxicol Pathol 29(4):467-478.
Abstract: http://www.ncbi.nlm.nih.gov/pubmed/11560252

Suwa T, Nyska A, Haseman JK, Mahler JF, Maronpot RR. 2002. Spontaneous lesions in control B6C3F1 mice and recommended sectioning of male accessory sex organs. Toxicol Pathol 30(2):228-234.
Abstract: http://www.ncbi.nlm.nih.gov/pubmed/11950166

Tangbanluekal L, Robinette CL. 1993. Prolactin mediates estradiol-induced inflammation in the lateral prostate of Wistar rats. Endocrinology 132:2407-2416.
Abstract: http://www.ncbi.nlm.nih.gov/pubmed/8504745



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