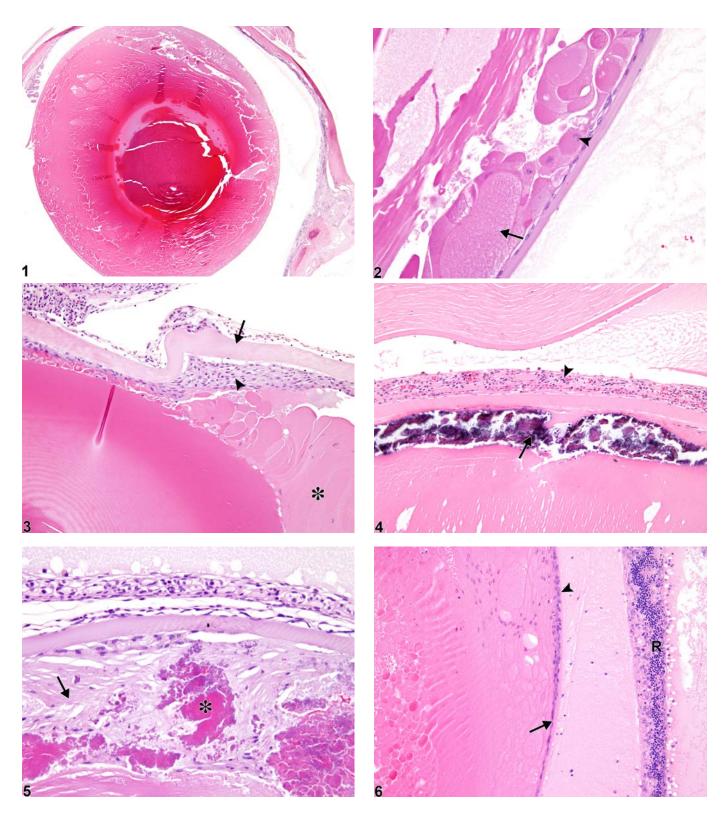




Eye, Lens – Cataract







Eye, Lens - Cataract

Figure Legend: Figure 1 Eye, Lens - Cataract in a female F344/N rat from a chronic study. There are lens fibers with separation, swelling, granularity, condensation, fragmentation, and disruption of the normally orderly configuration. Figure 2 Eye, Lens - Cataract in a male F344/N rat from a chronic study. There are swollen, disrupted lens fibers (arrow) with abnormal retention of lens fiber nuclei (arrowhead). Figure 3 Eye, Lens - Cataract in a male F344/N rat from a chronic study. There is capsular thickening and wrinkling (arrow), subcapsular anterior epithelial hyperplasia (arrowhead), and swollen, disrupted lens fibers (asterisk). Figure 4 Eye, Lens - Cataract in a female F344/N rat from a chronic study. There is subcapsular mineralization (long arrow) of the lens; posterior synechia of the iris (short arrow) is also present. Figure 5 Eye, Lens - Cataract in a male F344/N rat from a chronic study. Anterior subcapsular fibrosis (arrow) is intermixed with dark eosinophilic, fragmented lens fiber material (asterisk). Figure 6 Eye, Lens - Cataract in a male F344/N rat from a subchronic study. There is hyperplasia (arrowhead) and posterior migration (behind the lens bow) (arrow) of the anterior lens epithelium; there is also retinal degeneration and detachment (R).

Comment: A cataract is a lens opacity (capsular, subcapsular, anterior or posterior cortical, or nuclear) resulting from any cause, including heredity, trauma, metabolic disease, nutritional imbalance, environmental factors, increased intraocular pressure, aging, and excessive exposure to ionizing radiation or ambient light. Cataracts can also be concurrent with or secondary to other ocular disease, such as severe inflammation, iridial synechiae, and/or retinal degeneration. Incidental, spontaneously occurring cataracts of uncertain etiology are not uncommon in aging rats and mice.

Cataracts are characterized by lens fibers with various abnormal features, including separation, swelling, granularity, condensation, fragmentation, and disruption of the normally orderly configuration, as well as abnormal retention of lens fiber nuclei in several swollen lens fibers (Figure 1 and Figure 2). Swollen lens fibers with abnormally retained nuclei are sometimes referred to as "bladder" or "balloon" cells. Cataracts can also exhibit additional features, such as capsular thickening, wrinkling, and/or rupture (Figure 3) or lens fiber or capsular mineralization (Figure 4). Anterior epithelial cells of cataractous lens can also undergo proliferation and fibrous metaplasia (epithelial-to-mesenchymal transition) in response to injury. There may also be anterior subcapsular fibrosis (Figure 5) in a cataractous lens (note the intermixed dark eosinophilic, fragmented lens fiber material), as well as



Eye, Lens – Cataract

hyperplasia of the anterior epithelium of (Figure 6). The proliferative anterior epithelium may also extend posterior to the lens bow (posterior migration of lens epithelium) (Figure 6).

Recommendation: Cataracts should be diagnosed and assigned a severity grade. The site modifier "lens" should be included in the diagnosis (i.e., Eye, Lens - Cataract). If pertinent to the characterization of a treatment effect, the subtopographical localization of cataracts (subcapsular, cortical, nuclear, etc.) should be described in the pathology narrative but should not be included in the diagnosis. Morphologic features of cataracts (mineralization, fibrous metaplasia, bladder cells, etc.) should not be diagnosed separately, but should also be described in the narrative. Associated lesions (e.g., posterior synechia) should be diagnosed separately.

References:

Frame SR, Slone TW. 1966. Nonneoplastic and neoplastic changes in the eye. In: Pathobiology of the Aging Mouse, Vol 2 (Mohr U, Dungworth DL, Capen CC, Carlton WW, Sundberg JP, Ward JM, eds). ILSI Press, Washington, DC, 97-103.

Geiss V, Yoshitomi K. 1991. Eyes. In: Pathology of the Mouse: Reference and Atlas (Maronpot RR, Boorman GA, Gaul BW, eds), Cache River Press, Vienna, IL, 471-489.

Abstract: http://www.cacheriverpress.com/books/pathmouse.htm

Graw J. 2009. Mouse models of cataract. J Genetics 88:469-486.

Abstract: http://www.ncbi.nlm.nih.gov/pubmed/20090208

Greaves P. 2007. Nervous system and special sense organs. In: Histopathology of Preclinical Toxicity Studies: Interpretation and Relevance in Drug Safety Evaluation, 3rd ed. Academic Press, San Diego, CA, 861-933.

Abstract: http://www.sciencedirect.com/science/book/9780444527714

Hara A, Matsumoto M, Uga S. 1999. Morphological study on cataractogenesis of the Nakano mouse lens. Graefes Arch Clin Exp Ophthalmol 237:249-255.

Abstract: http://www.ncbi.nlm.nih.gov/pubmed/10090589

Kuno H, Usui T, Eydelloth RS, Wolf ED. 1991. Spontaneous ophthalmic lesions in young Sprague-Dawley rats. J Vet Med Sci 53:607-614.

Abstract: http://www.ncbi.nlm.nih.gov/pubmed/10845604

Newkirk KM, Chandler HL, Parent AE, Young DC, Colitz CMH, Wilkie DA, Kusewitt DF. 2007. Ultraviolet radiation-induced corneal degeneration in 129 mice. Toxicol Pathol 35:817-824. Full-text: http://tpx.sagepub.com/content/35/6/817.full



Eye, Lens – Cataract

References:

National Toxicology Program. 1996. NTP TR-452. Toxicology and Carcinogenesis Studies of 2,2-Bis(Bromomethyl)-1,3-Propanediol (FR-1138®) (CAS No. 3296-90-0) in F344 Rats and B6C3F₁ Mice (Feed Studies). NTP, Research Triangle Park, NC.

Abstract: http://ntp.niehs.nih.gov/go/6048

National Toxicology Program. 1997. NTP TR-450. Toxicology and Carcinogenesis Studies of Tetrafluoroethylene (CAS No. 116-14-3) in F344 Rats and B6C3F₁ Mice (Inhalation Studies). NTP, Research Triangle Park, NC.

Abstract: http://ntp.niehs.nih.gov/go/6044

National Toxicology Program. 2012. NTP TR-572. Toxicology and Carcinogenesis Studies of Methyl *trans*-Styryl Ketone (CAS No. 1896-62-4) in F344/N Rats and B6C3F1 Mice (Feed and Dermal Studies). NTP, Research Triangle Park, NC.

Abstract: http://ntp.niehs.nih.gov/go/36154

National Toxicology Program. 2012. NTP TR-579. Toxicology and Carcinogenesis Studies of N,N-Dimethyl-p-Toluidine (CAS No. 99-97-8) in F344/N Rats and B6C3F₁ Mice (Gavage Studies). NTP, Research Triangle Park, NC.

Abstract: http://ntp.niehs.nih.gov/go/37162

Okano T, Uga S, Ishikawa S, Shumiya S. 1993. Histopathological study of hereditary cataractous lenses in the SCR strain rat. Exp Eye Res 57:567-576.

Abstract: http://www.ncbi.nlm.nih.gov/pubmed/8282043

Rao GN. 1991. Light intensity-associated eye lesions of Fischer 344 rats in long-term studies. Toxicol Pathol 19:148-155.

Full-text: http://tpx.sagepub.com/content/19/2/148.full.pdf

Saika S, Kono-Saika S, Ohnishi Y, Sato M, Muragaki Y, Ooshima A, Flanders KC, Yoo J, Anzano M, Liu C-Y, Kao W W-Y, Roberts AB. 2004. Smad3 signaling is required for epithelial-mesenchymal transition of lens epithelium after injury. Am J Pathol 164:651-663.

Abstract: http://www.ncbi.nlm.nih.gov/pubmed/14742269

Shin EHH, Basson MA, Robinson ML, McAvoy JW, Lovicu FJ. 2012. Sprouty is a negative regulator of transforming growth factor β-induced epithelial-to-mesenchymal transition and cataract. Mol Med 18:861-873.

Abstract: http://www.ncbi.nlm.nih.gov/pubmed/22517312

Shinohara M, Masuyama T, Shoda T, Takahashi T, Katsuda Y, Komeda K, Kuroki M, Kakehashi A, Kanazawa Y. 2000. A new spontaneously diabetic non-obese Torii rat strain with severe ocular complications. Int J Exp Diabetes Res 1:89-100.

Abstract: http://www.ncbi.nlm.nih.gov/pubmed/11469401



Eye, Lens – Cataract

References:

Smith RS. 2002. Choroid, lens, and vitreous. In: Systematic Evaluation of the Mouse Eye: Anatomy, Pathology, and Biomethods (Smith RS, John SWM, Nishina PM, Sundberg JP, eds). CRC Press, Boca Raton, FL, 161-193.

Taradach C, Greaves P, Rubin LF. 1984. Spontaneous eye lesions in laboratory animals: Incidence in relation to age. Crit Rev Toxicol 12:121-147.

Abstract: http://www.ncbi.nlm.nih.gov/pubmed/6368130

Uga S, Tsuchiya K, Ishikawa S. 1988. Histopathological study of Emory mouse cataract. Graefes Arch Clin Exp Ophthalmol 226:15-21.

Abstract: http://www.ncbi.nlm.nih.gov/pubmed/3342971

Whiteley HL, Peiffer RL. 2002. The eye. In: Handbook of Toxicologic Pathology, 2nd ed, Vol 2 (Haschek WM, Rousseaux, CG, Wallig MA, eds). Academic Press, San Diego, CA, 539-584.

Williams DL. 2005. Ocular disease in rats: A review. Vet Ophthalmol 5:183-191.

Abstract: http://www.ncbi.nlm.nih.gov/pubmed/12236869

Yoshitomi K, Boorman GA. 1990. Eye and associated glands. In: Pathology of the Fischer Rat: Reference and Atlas (Boorman GA, Eustis SL, Elwell MR, Montgomery CA, MacKenzie WF, eds). Academic Press, San Diego, CA, 239-260.

Abstract: http://www.ncbi.nlm.nih.gov/nlmcatalog/9002563

Author:

Margarita M. Gruebbel, DVM, PhD, DACVP Senior Pathologist Experimental Pathology Laboratories, Inc. Research Triangle Park, NC